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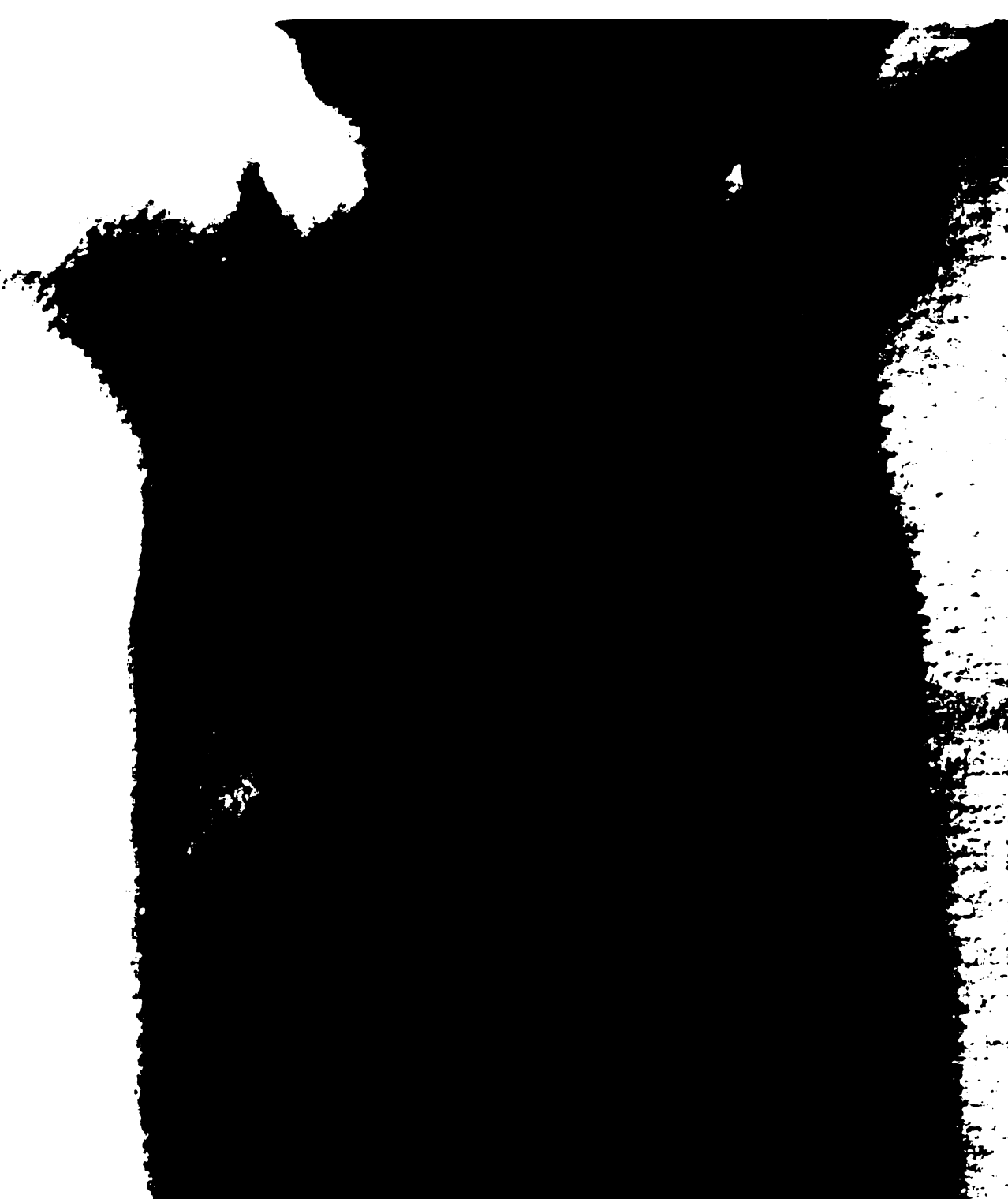
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## STUDIES ON INFANT NUTRITION

UNDER THE DIRECTION OF L. EMMETT HOLT, M.D., AND P. A. LEVENE, M.D.

### *II. The Hard or Casein Curds in Infants' Stools \**

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The casein curds in infant stools have been the subject of much discussion and controversy in recent years. Considerable disagreement exists in regard to both their chemical composition and the mechanism of their formation. All writers have been unanimous, however, in attributing to the curds much clinical significance, and in using them as a basis for choosing, or altering, the diet.

The older authorities regarded them as casein residues, appearing in the stools as the result of insufficient protein digestion and absorption. In recent years very emphatic protest against this view was expressed by Keller and Czerny.<sup>1</sup> According to their view, these curds were composed principally of a conglomeration of fat and soaps. Still more recently Biedert's<sup>2</sup> original view on the curds was revived, particularly by American writers. Selter,<sup>3</sup> Southworth and Schloss,<sup>4</sup> and Talbot<sup>5</sup> made chemical analyses of the curds and on the basis of his results reached the conviction that the principal component of these masses was undigested casein. The cause of their presence in the stools lay, according to these writers, in the disturbed protein digestion. Against this view there immediately arose opposition, led principally by the school of Finkelstein. L. Meyer and Leopold<sup>6</sup> did not deny the fact that the curds contained protein material, but, however, regarded the source of it not the casein of the ingested milk, but the intestinal secretions.

\*From the Laboratories of the Rockefeller Institute for Medical Research, and the Babies' Hospital, New York.

1. Czerny and Keller: *Des Kindes Ernährung*, etc., 1906, part 2, 17.

2. Biedert: *Jahrb. f. Kinderh.*, 1881, xvii, 251; *Kinderernährung im Säuglingsalter*, etc., 1905, ed. 5.

3. Selter: *Versamml. Deut. Naturforsch. u. Aerzte in Stuttgart* in 1907, 177.

4. Southworth and Schloss: *Arch. Pediat.*, 1909, xxvi, 4, 241.

5. Talbot: *Boston Med. and Surg. Jour.*, 1908, clviii, No. 24, p. 905; 1909, clx, No. 1, p. 13; 1910, clxii, No. 5, 134; *Arch. Pediat.*, 1909, xxvi, No. 12, p. 919.

6. Meyer, L. F., and Leopold: *Arch. Ped.*, 1909, xxvi, No. 10, p. 773; 1910, xxvii, No. 2, p. 126.

The cause of the appearance of the curds lay, according to the view of these writers, not in insufficient protein metabolism, but in faults of the carbohydrate assimilation and was brought about by excessive carbohydrate intake. These authors maintained that the appearance of the curds in the stools could be abated when the sugar intake was lowered.

Thus all writers are in agreement on one point, namely, that the presence of the hard curds in the stools is an indication of some fault of digestion, and that the health of the infant is in danger if the curds persist in the stools. The disagreements relate only to the interpretation of the nature of the disturbance and to the mode of treatment advocated by individual writers.

A mere superficial scrutiny of the literature on the subject reveals the fact that even the gravity of the symptom has never been firmly established; it was an assumption based on speculative considerations. Taking this assumption for granted, the individual observers applied their efforts in search for a method of treatment by which the symptom could be abated. The interpretation of the pathogenesis of the symptom was then determined by the success or failure of a certain mode of treatment. Thus, if the removal, complete or partial, of carbohydrate from the diet led to the disappearance of the curds, the theory was advanced that the disturbance of carbohydrate digestion was the basic cause of this symptom. Arguments of this nature can scarcely be regarded as very convincing. On the other hand, it was never clearly demonstrated that there existed a definite form of indigestion which invariably resulted in the curd formation in the stools, and still less evidence existed in favor of the assumption that the nutrition of the infants was affected severely in the periods when the stools contained the curds in abundance.

New experimental inquiry was needed in order to obtain reliable information on all these questions, and the present work was stimulated by such considerations.

Thus it is natural that the work should fall into two parts, one dealing with the relation of the curds to the state of digestion, and the second to that of nutrition. Information relating to the first part of the problem was sought on the grounds of the following reasoning: If the curds represent the remnants of undigested food, then their composition should be determined by the nature of the digestive insufficiency. Thus, if the curds consist principally of one component, of protein, of fat, or of carbohydrate, the conclusion would follow that there existed an insufficiency in the digestive capacity for that food-stuff. If that were so, one should also find that the composition of the entire stool showed a preponderance of that same component. On the other hand, should the curds have exactly the composition of normal stools differing only in the water content, the assumption may be justified that their formation

is conditioned by irregularities of peristalsis. Finally the mass of the stools may, under some forms of indigestion, acquire such peculiarities of composition as would lead to the separation of one of its constituents in solid form. Thus, the accumulation of calcium salts may result in separation of lime-soaps; unusually high acidity may bring about precipitation of nucleins. Under such conditions one should expect the curds to have a composition distinctly different from that of the remainder of the stools, but would expect also a definite constant composition of the stool as a requirement for the curd formation.

From these considerations it is evident that it is not sufficient to limit the chemical investigation to the composition of the curds except when it is desired to establish the relationship between the state of digestion and the curd formation. On the contrary, it is very essential to supplement the analysis of the curds by that of the total stools. Furthermore, the insufficiency of the digestive organs may be essentially quantitative in its nature. That is, it may occur only after the intake of a certain constituent of the daily diet has overstepped a certain limit. Thus in order to be able to take into account all the factors engaged in the curd formation it is necessary to possess the knowledge of the chemical composition of the food, of the curds, and of the total stool in which they occur.

The data furnished by such analyses suffice to bring to light the bearing of any gastro-intestinal disturbance on curd formation, but they cannot help to interpret the influence of the curd formation on the state of general nutrition. It has been stated that there exists no experimental evidence in support of the view that the curds in infants' stools are indicative of some serious disturbance of nutrition. And yet the importance of the entire problem of curd formation depends on the answer to this question. In order to approach the solution of this problem the analyses of the food, of the curds, and of the total stools were supplemented by that of the urine, so that at least in regard to the nitrogen the exact daily balance could be established. Taking into account, in addition to this, the curve of the daily gain in weight, one can obtain fair information as to the general state of nutrition during the periods when the stools showed the greatest number of curds.

One other possibility needs to be analyzed before the discussion on the significance of the curds is exhausted, namely: Assuming that the curds represent a part of the ingested food which escaped digestion, one can easily recognize that the gravity of this condition would depend on the proportion of the food which escapes in that form. If the loss is considerable then normal nutrition could be maintained only by a corresponding increase in the daily diet. This information can be obtained by an estimation of the quantities of food elements contained in all the

curds present in a twenty-four-hour sample of the stools. Naturally the curds have to be cleansed very carefully from the adhering feces. Such analyses were carried out in the course of the present investigation. They are recorded in Table 2.

Before passing to the report on the results of the present investigation it seems necessary to describe the general character of the curds, which are referred to in the present communication. It has been pointed out by several writers that much of the controversy in regard to the significance of the curds has resulted from the fact that writers were not sufficiently explicit in describing the appearance and the physical properties of the curds, and while some were dealing actually with fat-curds, other writers had under their observation curds of an entirely different composition. The curds referred to in the present paper possessed great similarity in their physical properties, though they differed considerably in their form.

*Physical Character of the Curds.*—Very commonly they consisted of rather hard, round or oval, not infrequently bean-shaped masses. Often they presented masses tapering at one end, or flattened into thin plates. The surface was generally smooth. The size varied from small fragments to masses more than an inch in length. The weight of such curds reached 2 gm. In several cases the combined curds obtained from a twenty-four-hour sample of feces (three or four large and two or three smaller masses) weighed between 7 and 8 gm. The surface was frequently stained deep yellow, while the inner part was usually white or cream-colored, more rarely yellow. In a few instances they presented a shining surface, persistent even after careful washing. Very often more or less numerous small fragments of the same material as the hard curds were found in the stools, either with or without the larger masses, possibly resulting from disintegration of the latter. These hard curds have the common characteristic of being more or less tough and resistant to pressure, and can thus be distinguished from the so-called fat-curds. The latter are generally soft and small in size.

On one occasion there was obtained a smooth, oval, moderately hard mass about  $1\frac{1}{4}$  inches in length, which became liquid during the drying on a water-bath. On analysis it was found to contain over 80 per cent. of fat and between 1 and 2 per cent. nitrogen. Macroscopically it differed from the typical hard curds only in yielding more readily to pressure and in showing a smoother texture. The feces of the same child contained for a long period previous to that day the characteristic casein curds.

*Chemical Composition.*—Results of complete analysis of the curds are recorded by Selter<sup>4</sup> and by Talbot.<sup>5</sup> The total number of samples analyzed was eight, one by Selter and seven by Talbot. In regard to the protein content, there was an approximate uniformity in all the

Description of Stools Containing Curds

Number	Name	Date	Food Composition *							Composition of Curds Per Cent. of Dried Weight of Curds				Description of Stools Containing Curds
			Protein, Per Cent.	Fat, Per Cent.	Carbohydrate, Per Cent.	Nitrogen, gm.	Fat, gm.	Carbohydrate, gm.	Total Calories	Nitrogen	Protein	Fat	Ash	
1.	E. A.	Nov. 1910	51.75	...	5	3.02	....	54.0	334	9.8	61.2	20.0	...	Pasty; granular, yellow-green.
2.	A. P.		91.2	1.4	6	2.02	14.7	63.0	465	10.5	65.6	22.5	4.8	Pasty; granular, green-yellow, sour.
3.	S. R.	Dec.	261.4	1.6	5.7	2.35	16.8	59.9	487	10.6	66.2	25.1	...	Loose; granular, green.
4.	W. E.		72.3	.9	2.6	3.31	8.1	23.4	304	10.6	66.2	22.3	4.8	Loose-watery; granular, green.
5.	H. C.		71.8	.9	5	2.72	8.5	47.2	376	11.3	70.5	....	6.5	Pasty; granular, with mucus, green-yellow.
6.	H. S.		71.8	.9	2.25	3.03	9.5	23.6	307	10.6	66.2	19.0	4.8	Pasty; smooth-granular, green-yellow.
7.	P. C.		121.6	1.8	7.8	2.42	17.0	73.6	544	9.9	61.8	29.5	5.0	Pasty; smooth, pale yellow-green, sour.
8.	I. W.		161.4	1.6	5.7	2.35	16.8	59.9	487	9.5	59.3	....	...	Pasty; smooth-granular, yellow-green.
9.	T. S.		201.75	2.0	5	3.03	21.6	54.0	538	9.0	56.2	22.0	4.8	Pasty; smooth, yellow becoming green-brown, sour.
10.	T. S.		211.75	2.0	5	3.03	21.6	54.0	538	8.8	54.9	22.0	4.8	Loose-pasty; granular, green and yellow.
11.	T. B.	Mar. 1911	301.4	1.6	5	2.35	16.8	52.5	459	10.1	63.1	....	4.8	Pasty; granular, yellow becoming green.
12.	C. R.	7-8	2.05	...	2.65	3.45	....	27.8	251	11.4	71.2	18.8	...	Loose; smooth, with mucus, yellow-brown becoming green.
13.	J. H.	13-14								9.4	58.7	22.0	...	Pasty; smooth, pale gray-yellow, slightly green.
14.	J. H.	14-15	2.0	2.9	5	3.54	32.1	55.3	663	10.1	63.1	....	...	Loose-pasty; smooth, pale yellow, slightly green.
15.	J. H.	17-21	2.0	1.8	5	3.54	19.9	55.3	549	9.4	58.7	....	...	Loose-pasty; mostly smooth, green-yellow and yellow-gray.
16.	J. H.	21-22	2.2	2.0	5	4.07	23.1	57.7	609	8.8	54.9	....	...	Loose-pasty; smooth, yellow becoming white-gray and pale green.

\*Food

- No. 1. Fat-free milk 50 per cent., lime-water 5 per cent., barley-water 45 per cent., lactose 5 per cent. Food boiled.  
 2. Milk 35 per cent., lime-water 5 per cent., barley-water 60 per cent., lactose 5 per cent., and 12 c.c. malt-soup extract.  
 3. Milk 40 per cent., lime-water 5 per cent., barley-water 55 per cent., lactose 5 per cent., and 8 c.c. malt-soup extract.  
 4. Mixture of full milk, fat-free milk, 5 per cent. lime-water and barley-water making milk fat 0.9 per cent., lactose 2.6 per cent.  
 5. Skimmed milk 50 per cent., lime-water 5 per cent., barley-water 45 per cent., lactose 5 per cent.  
 6. Skimmed milk 50 per cent., lime-water 5 per cent., barley-water 45 per cent., lactose 2.25 per cent.  
 7. Milk 45 per cent., lime-water 5 per cent., barley-water 50 per cent., lactose 5 per cent., 30 c.c. malt-soup extract.  
 8. Milk 40 per cent., lime-water 5 per cent., barley-water 55 per cent., lactose 5 per cent., 8 c.c. malt-soup extract.  
 9. Milk 50 per cent., lime-water 5 per cent., barley-water 45 per cent., lactose 5 per cent.  
 10. Same as in No. 9.  
 11. Milk 40 per cent., lime-water 5 per cent., barley-water 55 per cent., lactose 5 per cent.  
 12. Fat-free milk 55 per cent., lime-water 5 per cent., water 35 per cent., lactose 2.65 per cent.  
 13 and 14. Mixture full milk, fat-free milk, lime-water 5 per cent., and barley-water making milk fat 1.8 per cent., lactose 5 per cent., olive-oil 12 c.c.  
 15. Same as in Nos. 13 and 14, with olive-oil omitted.  
 16. Similar mixture to that in preceding numbers, but making milk fat 2 per cent, lactose 5 per cent.

curds. Regarding the fat content Talbot recorded a considerable variation in different samples. According to this observer, the fat content of the curds was determined by that of the food. In the course of the present observations more than thirty samples of curds were analyzed. Great care was taken to free the curds from adhering feces. This was accomplished by shaking them with water. The wash waters were removed by decantation, and the curds dried and used for analysis. The chemical analysis of these masses revealed a similarity in their composition which cannot be regarded as accidental. It is clearly seen from the tables that the protein, fat and ash content fluctuated within very narrow limits.

On the other hand, the composition of the stools was very variable, the nitrogen content fluctuating between 3, 4 and 5 per cent., only in one instance reaching 5.5 per cent., and in another 6 per cent.; the proportion of fat varied from 26 to 48 per cent., the ash between 20 and 31 per cent. The total acidity of the feces and the content of volatile acids also presented great variations.

Thus it is evident that the hard curds are composed differently than the mass of the stools and not infrequently contain more than 75 per cent. of protein. On this ground they cannot be regarded as masses of feces compressed into the peculiar formations owing to some irregularities of intestinal motility. They therefore represent either remnants of food that escaped normal digestion, or a normal component of the feces separated out of the mass of the stools owing to some peculiarity of the composition of the latter. The fact that the chemical nature of the feces that contained the curds differed very markedly lends more support to the first of the two hypotheses, namely, that the curds represent remnants of undigested food, principally protein.

This naturally leads the inquiry into the causes of this partial indigestion. It has to be admitted that a very definite answer to this question cannot be given notwithstanding all the data furnished by the present work.

The great variations in the chemical composition of the stools which show the presence of curds argue against the assumption that there exists one definite form of indigestion which brings about the curd formation. To the same conclusion one is led by the analysis of the influence of diet on the appearance of curds. It is clearly seen from Table 1 how varied the diet may be which renders possible the formation of curds in the feces. And still the impression is gained that the protein intake is a very significant factor in bringing about this symptom. Particularly the metabolism experiment on Daniel L. seems to furnish evidence in support of this view. This patient was under observation for considerable time and his diet was altered several times. It was observed that the curds



Number	Name	Date	Food Composition *							Dried Weight of Stools, Including Curds, gm.	Dried Weight of Curds, gm.	Output, Per Cent. of Dried Weight of Curds				Description of Stools Containing Curds
			Protein, Per Cent.	Fat, Per Cent.	Carbohydrate, Per Cent.	Nitrogen, gm.	Fat, gm.	Carbohydrate, gm.	Total Number (Stools)							
1.	D. L.	Dec. 1910	2.1	1.8	5	4.58	24.6	68.3	686	12.13	1.00	9.0	56.2	23.3	...	Pasty; constipated, smooth, yellow-gray
2.	D. L.	6-7								17.82	3.60	10.1	63.1	23.3	...	Loose-pasty; smooth, yellow, green flakes.
3.	D. L.	7-8								11.20	2.85	10.2	63.7	24.0	4.6	Pasty; smooth, yellow becoming green.
4.	D. L.	12-13								9.88	1.00	10.4	65.0	24.0	4.6	Pasty; constipated, smooth, yellow becoming gray-brown.
5.	D. L.	13-14	1.8	1.2	5	3.94	16.4	68.3	582	11.18	2.80	11.0	68.7	24.0	4.6	Pasty; part granular, yellow becoming green, part smooth, brown.
6.	D. L.	15-16								6.02	.70†	1.3	8.1	81.5	14.7	Pasty; constipated, smooth, yellow becoming gray-brown, with mucus, small hard curds and one large fat lump.
7.	D. L.	17-18								6.30	.45	10.9	68.1	24.0	4.6	Pasty; smooth, yellow becoming gray-brown.
8.	D. L.	18-19								8.69	.30	11.5	71.9	19.6	6.3	Pasty; constipated, smooth, yellow becoming gray-brown.
9.	R. M.	14-15	1.8	1.2	5	3.33	13.9	57.8	492	13.84	.90	10.9	68.1	19.6	6.3	Pasty; constipated, smooth, yellow becoming gray-brown.
10.	R. M.	16-17								5.58	.10	10.9	68.1	19.6	6.3	Pasty; constipated, smooth, yellow becoming gray-brown and slightly green.
11.	R. M.	18-19								10.63	3.15	10.5	65.6	30.0	4.0	Pasty; finely granular, smooth, yellow becoming green, sour.
12.	J. D.	7-8								10.33	2.90	10.0	62.5	30.0	4.0	Pasty; partly granular, smooth, yellow becoming green, partly smooth, yellow becoming white.
13.	J. D.	9-10	2.1	1.8	5	3.53	18.9	52.5	527	8.92	3.65	10.8	67.5	30.0	4.0	Pasty; smooth, yellow becoming gray-brown.
14.	J. D.	12-13								6.22	1.30	11.5	71.9	30.0	4.0	Pasty; mostly granular, yellow becoming green, partly smooth, yellow becoming white and green.
15.	J. D.	14-15								6.23	1.55	10.5	65.6	30.0	4.0	Pasty; smooth, green and yellow, becoming brown and green.
16.	J. D.	17-18								10.98	4.65	11.1	69.3	30.0	4.0	Pasty; part smooth, yellow becoming brown, white and green, part granular, green and sour.
17.	J. D.	18-19	1.8	1.2	5	3.33	13.9	57.8	492	6.67	2.55	10.6	66.2	30.0	4.0	Pasty; part smooth, yellow becoming green and brown, part granular and green.
	J. D.															

\*Food.—Nos. 1, 2, 11, and 12.—Mixture full milk, fat-free milk, 5 per cent. lime-water and water making milk fat 1.8 per cent.; lactose 5 per cent.

In all other numbers, mixture full milk, fat-free milk, 5 per cent. lime-water and water making milk fat 1.2 per cent.; lactose 5 per cent.

†Fat lump only, small hard curds not separated from stool.

appeared in the highest number and more continually when the percentage of protein intake reached the highest values. The only period when the stools were free from curds was when both the fat and protein intake were low and the carbohydrate intake comparatively high. The variation in fat intake alone remained without influence on the curd formation.

TABLE 3.—COMPOSITION OF STOOLS CONTAINING HARD CURDS—FECES WITHOUT THE CURDS

Name	Date	Total Nitrogen, gm.	Per Cent. of Dried Weight of Feces					Soap Fat, Per Cent. of Total Fat	C.c. N/10 NaOH Equivalent				
			Nitrogen	Protein	Fat	Soap Fat	Ash		Total Acidity of Feces	Volatile Acids of Feces	100 gm. Dried Weight Feces		
											Total Acidity	Acids Volatile	
	Dec. 1910												
D. L.	6-7	.592	4.9	30.6	29.7	19.2	26.4	64.6	45.2	103.5	406	930	
D. L.	7-8	.782	5.5	34.4	30.4	11.4	22.6	85.2	85.2	112.9	599	794	
D. L.	12-13	.278	3.4	21.2	45.0	25.3	19.8	56.3	38.9	44.8	804	1,010	
D. L.	13-14	.531	6.0	37.5	36.9	17.5	25.9	42.3	17.7	172.9	199	1,947	
D. L.	15-16	.407	4.8	30.0	36.2	16.3	25.2	45.2	6.8	47.6	354	2,386	
D. L.	17-18	.226	4.3	26.8	33.6	16.6	24.2	49.3	3.4	47.3	121	1,771	
D. L.	18-19	.282	4.8	30.0	36.9	17.5	25.9	42.3	4.9	88.3	83	1,510	
R. M.	14-15	.376	4.5	28.1	33.6	25.3	29.4	75.3	8.4	179.9	100	2,144	
R. M.	16-17	.618	4.8	30.0	33.6	25.3	29.4	75.3	4.1	36.8	52	437	
R. M.	18-19	.285	5.2	32.5	33.6	25.3	29.4	75.3	5.7	43.7	104	798	
J. D.	7-8	.288	3.8	23.8	46.2	26.3	20.9	56.9	33.6	77.8	448	1,040	
J. D.	9-10	.311	4.2	26.2	43.0	31.2	21.2	72.6	31.4	92.7	422	1,248	
J. D.	12-13	.230	4.4	27.5	48.8	38.7	21.4	79.3	10.2	83.3	332	2,724	
J. D.	14-15	.198	4.0	25.0	37.7	19.7	25.1	52.2	12.0	65.2	569	3,697	
J. D.	15-16	.236	5.1	31.8	36.3	24.5	19.3	67.5	20.2	58.1	580	1,909	
J. D.	17-18	.263	4.3	26.8	45.1	33.9	22.8	75.3	4.7	30.0	236	1,736	
J. D.	18-19	.201	4.7	29.4	38.1	26.6	20.3	69.8	7.7	68.8	354	3,533	
	March, 1911												
J. H.	13-14	.141	4.5	28.1	26.8	15.8	26.4	59.0					
J. H.	14-15	.164	4.3	26.8	32.4	19.2	31.2	59.3					
J. H.	17-18	.094	3.8	23.8	48.6	35.9	25.3	73.9					
J. H.	18-19	.170	4.1	25.6	31.5	13.2	22.5	41.9					
J. H.	19-20	.136	3.9	24.4	28.0	8.1	23.0	23.9					
J. H.	20-21	.245	3.8	23.8	35.4	16.7	28.3	47.2	17.5	44.8	270	693	
J. H.	21-22	.247	3.3	20.6	48.3	5.0	24.2	10.4	23.1	72.4	311	976	
J. H.	22-23	.123	3.7	23.1	39.8	15.9	20.6	39.9					

Thus it seems probable that under a variety of conditions, part of the protein intake escapes being digested and is removed by the stools in form of hard curds. The real mechanism of the curd formation is not easy to interpret for the reason that normally protein enters the intestinal canal from the stomach in a state of solution, and even if some of it enters in solid form the proteolytic enzymes of the pancreas are capable of bringing it into solution. If the protein is of the nature of a nuclein or paranuclein, as, for instance, casein, the alkalies present in the intestinal tract should be capable of effecting its solution. There is undoubt-

edly a sufficient supply of proteolytic enzymes in the intestinal canal even under the conditions favorable to abundant curd formation, for the reason that often only a comparatively small part of the ingested protein appears in the stools in that form, the greatest part having apparently undergone normal digestion. Thus there must be some factors at play, which prevent the enzymes from penetrating the curd. No definite explanation of their nature can be offered at the present moment.

TABLE 4.—COMPOSITION OF STOOLS CONTAINING HARD CURDS—FECES INCLUDING THE CURDS

Name	Date	Feces. Dried Wt. in gm.		Total Nitrogen, gm.	Total Fat, gm.	Total Ash, gm.	Per Cent. of Dried Weight of Feces			
		With Curds	Without Curds				Nitrogen	Protein	Fat	Ash
	Dec. 1910									
D. L.	6-7	12.13	11.13	.682	3.53	2.99	5.6	35.0	29.3	24.6
D. L.	7-8	17.82	14.22	1.146	5.16	3.61	6.4	40.0	28.9	20.3
D. L.	12-13	11.20	8.35	.567	4.47	1.79	5.1	31.9	39.9	16.0
D. L.	13-14	9.88	8.88	.635	3.52	2.35	6.4	40.0	35.7	23.8
D. L.	15-16	11.18	8.38	.719	3.72	2.24	6.4	40.0	33.3	20.0
D. L.	17-18	6.02	5.32*	.235	2.37	1.39	3.9	24.4	39.3	23.0
D. L.	18-19	6.30	5.85	.331	2.27	1.53	5.3	33.1	36.1	24.4
R. M.	14-15	8.69	8.39	.411	2.88	2.48	4.7	29.4	33.2	28.5
R. M.	16-17	13.84	12.94	.716	4.52	3.85	5.2	32.5	32.6	27.8
R. M.	18-19	5.58	5.48	.296	1.86	1.62	5.3	33.1	33.3	28.9
J. D.	7-8	10.63	7.48	.619	4.41	1.70	5.8	36.2	41.3	15.9
J. D.	9-10	10.33	7.43	.603	4.07	1.69	5.8	36.2	39.3	16.3
J. D.	12-13	8.92	5.27	.625	3.67	1.28	7.0	43.7	41.1	14.3
J. D.	14-15	6.22	4.92	.347	2.21	1.30	5.6	35.0	35.6	20.8
J. D.	15-16	6.23	4.68	.399	2.16	.970	6.4	40.0	34.7	15.5
J. D.	17-18	10.98	6.33	.775	4.14	1.67	7.0	43.7	37.8	15.2
J. D.	18-19	6.67	4.12	.471	2.30	.920	7.1	44.4	34.5	13.8
	March, 1911									
J. H.	13-14	4.05	3.15	.225	1.042	.882	5.6	35.0	25.7	21.7
J. H.	14-15	4.55	3.80	.239	1.396	1.225	5.3	33.1	30.7	27.0
J. H.	17-18	3.20	2.50	.161	1.295	.670	5.0	31.2	40.4	20.9
J. H.	18-19	4.70	4.20	.217	1.380	.973	4.6	28.8	29.4	20.7
J. H.	19-20	4.20	3.50	.201	1.057	.844	4.8	30.0	25.2	20.1
J. H.	20-21	6.88	6.48	.282	2.340	1.853	4.1	25.6	34.0	27.9
J. H.	21-22	7.91	7.41	.291	3.632	1.818	3.7	23.1	46.0	23.0
J. H.	22-23	3.45	3.35	.132	1.343	.696	3.8	23.8	38.9	20.2

\*Fat lump only separated, few small hard curds left in the feces.

It remains to discuss the data regarding the practical significance of the symptom. It has been stated before that the curds represent part of the food that has escaped being digested. It naturally follows that the injury occasioned by it to the economy of the organism may be very perceptible when the proportion of the non-utilized fraction reaches a high value. The review of Table 2 clearly demonstrates that such may be the case only on very rare occasions. Thus it is seen that out of seventeen stools, in nine the curds contained less than 1 gm. and not more

than 1.5 gm. of dry material. Calculating their protein content at 65 per cent., the loss of protein occasioned by the curd formation in these nine instances ranged between 0.06 and 0.95 gm. in twenty-four hours. In four stools the total dry weight of the curds reached from 2.0 to 3.0 gm. This resulted in a protein loss varying between 1.35 and 2.0 gm. in twenty-four hours. In four other stools the dry weight of the curds was between 3.15 and 4.65 gm., which meant a loss of protein of from 2 to 3 gm. Calculating the twenty-four-hour intake at 20 gm., it becomes evident that only on very few occasions was the loss resulting from the curd formation considerable. Generally, however, the appearance of curds in stools in itself does not lead to a perceptible decline in the utilization of the food-stuffs.

Furthermore, this conclusion is corroborated by the metabolism experiments. It is seen from Table 5 that the largest mass of curds was formed in the fifth period, which coincided with the period of the largest nitrogen retention. Of the two periods, fourth and fifth, with about equal protein intake, the mass of the curds was greater when the carbohydrate intake was of a lower, and the fat intake of a higher value. Comparing further the calorific value of the diet of the fourth and fifth periods, in which the protein intake was unchanged, one notices that in the fourth period the food utilization was less perfect, and yet it led to the formation of a smaller mass of curds.

On the other hand, the stools were completely free from lumps in the second period. In that period the food intake was of a comparatively lower calorific value, and in proportion to other food-stuffs rich in carbohydrates and very poor in protein. The retention of nitrogen in that period was very insignificant. In other words, the state of nutrition was in a less perfect condition when the stools were free from curds.

#### CONCLUSIONS

1. The "hard" or "casein" curds represent remnants of food, principally of protein nature, that have escaped being digested.
2. The exact mechanism of their formation as yet cannot be ascertained and they should be regarded as a peculiarity appearing in course of imperfect conditions of digestion.
3. The curds are not pathognomonic of any definite pathologic condition.
4. The loss of food occasioned by their formation and the impairment of the general nutrition resulting from it is insignificant.
5. In attempting to correct the state of digestion one should be guided by the general rules of infant feeding, paying only secondary attention to the appearance or disappearance of curds from the stools.

TABLE 5.—DANIEL L. PROTEIN RETENTION\*

Number	Date	Intake in gm.			Intake in Per Cent.			Output.		Daily Average Nitrogen				Average Daily Gain in Weight	Description of Feces
		Carbohydrate, gm.	Fat, gm.	Nitrogen, gm.	Carbohydrate, Per Cent.	Fat, Per Cent.	Protein, Per Cent.	Intake in Calories, Total Number	Urine, gm.	Feces, gm.	Absorbed, gm.	Retained, gm.	Absorbed, Per Cent.	Retained, Per Cent.	
	Oct. 1910														
1.	16-25	55.34	16.1	2.100	5.0	1.4	1.2	453	1.496	0.456	1.651	0.155	78.3	9.4	— 3.9 Partly pasty, smooth, gray-yellow and brown-yellow, partly watery, granular, green-brown. Hard curds present on three days.
2.	25-28	73.85	14.5	1.759	6.0	1.2	1.0	495	1.377	0.321	1.438	0.061	81.8	4.2	+12.3 Mostly formed and brown; a little thinner and green-brown. No hard curds present.
3.	Nov. 8-15	95.0	27.4	3.618	7.4	2.2	2.0	776	1.651	0.946	2.672	0.981	84.5	32.1	+28.7 Partly formed, smooth, brown; partly thinner, granular, yellow. Hard curds present on four days.
4.	15-22	84.04	18.0	4.831	6.3	1.0	2.55	695	3.201	0.809	4.022	0.821	83.3	20.4	+15.1 Like the feces of preceding period, generally more watery. Hard curds present every day, often large curds.
5.	Dec. 6-10	56.05	20.5	4.765	5.0	1.8	2.1	608	2.709	1.005	3.760	1.051	77.9	28.3	— 7.6 Mostly loose-watery (first day only formed), granular, with mucus, green-yellow, many large hard curds, some present every day.

No.

\*Composition of Food

1. 35 per cent. milk, 5 per cent. lime-water, 60 per cent. water, milk-sugar to 5 per cent.
2. 30 per cent. milk, 5 per cent. lime-water, 65 per cent. barley water, milk-sugar to 5 per cent., 12 c.c. malt-soup extract.
3. 55 per cent. milk, 5 per cent. lime-water, 40 per cent. water, milk-sugar to 5 per cent., 30 c.c. malt-soup extract.
4. Fat-free milk 20 per cent., skimmed milk 55 per cent., lime-water 5 per cent., water 20 per cent., milk-sugar to 5 per cent., 16 c.c. malt soup extract.
5. Fat-free milk and full milk, 5 per cent. lime-water and water to make milk fat 1.8 per cent., milk protein 2.1 per cent., milk-sugar to 5 per cent.

After the present communication was completed for publication there appeared a paper by Brennemann<sup>7</sup> on the etiology and nature of hard curds. On the basis of many observations the author was led to the conclusion that curds appear in stools only after feeding on raw milk, and that the curds disappear as soon as the diet is changed to boiled milk. Brennemann takes for granted that the appearance of curds is the result of a serious fault of digestion, which can be corrected by changing the diet from raw to boiled milk. The observations of Brennemann may prove of practical and theoretical importance, but his work fails to furnish new information as to the clinical significance of the appearance of the curds. The present observations may be of some value whether or not the views of Brennemann are corroborated.

Without any desire to contradict, or to disagree with the views expressed by this writer, attention may be called to the fact that the first patient under our observation was fed on boiled milk.

#### METHODS OF ANALYSIS

*Total Nitrogen* was determined by the Kjeldahl-Gunning method. Samples of food mixtures, feces, and curds were dried on a water bath and then to constant weight in an air bath.

*Sugar* estimation was made volumetrically by the method described by Ettore Selvatici.<sup>8</sup> The procedure was the following: The proteins of the milk were removed by coagulation, and the clear filtrate was added from a burette into a definite volume of a boiling Fehling's solution. A small amount of potassium ferrocyanid is added to Fehling's solution previous to the beginning of titration. The sugar solution is added until the Fehling solution loses its blue color.

*Starch* content in barley water, barley jelly, and bean gruel was determined by its inversion into glucose. This was accomplished by heating the solution with dilute sulphuric acid in an autoclave. The sugar was titrated by the Pavy method.

*Fat* estimation was made by extraction with ether in a Soxhlet apparatus. For the determination of the total fat, the substance to be extracted was carefully mixed with phosphoric acid. Fat exclusive of soap fat was estimated directly on the unmixed feces. In the food, fat was estimated by extracting with ether in a Soxhlet apparatus. In order to remove the moisture from the ether extracts, the residues of these extracts were redissolved in chloroform, filtered through paper moistened with chloroform, and dried first on a water bath and then in a desiccator.

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7. A Contribution to Our Knowledge of the Etiology and Nature of Hard Curds in Infants' Stools, *AM. JOUR. DIS. CHILD.*, 1911, i, 341.

8. Selvatici, Ettore: *Bul. de l'Assn. des Chimistes de sucrerie et de distillerie*, 1910, xxvii, 1179.

*Ash-Estimation.*—The dry samples of food or excretions were incinerated and the residue extracted with hydrochloric acid. The insoluble part was further ignited with the use of a few drops of strong nitric acid. The acid filtrate was added to the residue and evaporated to dryness.

The total acidity and volatile acids in the feces were determined in the following way: A known proportion of the moist feces was made into an emulsion by shaking in distilled water with glass beads, and then made to definite volume. An aliquot part was titrated for total acidity with decinormal sodic hydrate, phenolphthalein being used as indicator. To determine volatile acids, another portion of the emulsion was made acid to congo paper with dilute phosphoric acid and distilled with steam into a measured quantity of decinormal sodic hydrate until the dropping distillate was no longer acid; the unneutralized sodic hydrate then being titrated with decinormal sulphuric acid and phenolphthalein used as indicator.

#### HISTORIES

Daniel L., 7 months old, was admitted to the hospital Oct. 5, 1910. There was a history of protracted diarrhea and no gain in weight. He weighed 10 pounds, 8 ounces and was poorly nourished. Metabolism experiments were carried on from October 15 through October 28, from November 8 through November 22, and from December 6 through December 10, and the stools were collected for analysis until December 19. During the first period the weight was variable, being about the same at the end as at the beginning, 4,722 gm. The temperature was also variable. During the second period the child was looking well and the weight increased rather steadily from 5,003 grams to 5,310 grams. In the last period the weight was again variable, showing a slight loss at the end of the metabolism experiment and a small increase during the following days in which the stools were collected. During this time the child had low, irregular fever due to a cervical adenitis, which continued for some time after the conclusion of the experiment, accompanied by loose stools and falling weight. Subsequently the food was changed to one with less fat and protein and high carbohydrate with marked improvement and gain in weight.

Richard M., 2½ months old, was admitted to the hospital Sept. 6, 1910. He had not been gaining weight, and for ten days had had diarrhea with fever and some vomiting. He was poorly nourished but not emaciated, weighing 9 pounds, 6 ounces. He was used as a control for the Daniel L. experiments, his stools being collected from October 16 through October 28, November 8 through November 22, and December 6 through December 19. During all this time he showed a generally rising weight-curve, from 4,527 gm. on October 16 to 5,063 gm. on December 19. After the first period the stools were very good, though they frequently contained small hard curds, rarely large or numerous ones. He was discharged December 25, gaining and in good condition.

John D., 2½ months old, was admitted to the hospital Sept. 27, 1910, with a history of diarrhea and loss in weight. He was emaciated and rachitic. His weight was 5 pounds, 11 ounces. He began to gain almost at once and his stools improved. Successive increases were made in his food as his weight became stationary, on October 11, October 22, November 8, November 16, and November 23. Between November 8 and November 16 a peri-rectal abscess formed and he had fever but still continued to gain in weight. December 3 large hard curds began to appear in his stools. From December 6 through December 19 the stools were collected for analysis. During this time his stools were generally good, though they contained many large hard curds, and his weight increased from

3,508 gm. December 6 to 3,584 gm. December 18. Double otitis media developed from December 5 and erysipelas of the scalp from about December 18, with more or less fever, and he began losing weight. He was well of the erysipelas by December 29, but one ear was still discharging at that time. The gain in weight began when he was placed on a milk formula with low fat and protein and relatively high sugar.

Joseph H., 9 months old, was admitted to the hospital Feb. 6, 1911, weight 8 pounds,  $3\frac{1}{2}$  ounces. There was a history of constipation and considerable colic, and recently, vomiting and loss of weight. He was rather poorly nourished. There was no vomiting after admission but his weight remained at a standstill until February 24, when his food was increased. He served as a metabolism control from March 14 through March 23. During the experiment he gained slightly in weight, from 3,955 gm. to 3,994 gm. and had good stools, which, however, invariably contained hard curds, often large and numerous ones. He continued to gain in weight and have good stools and was discharged April 23, weighing 4,583 gm.



## THE CALCIUM METABOLISM IN INFANTILE TETANY, WITH REPORT OF A CASE \*

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Before discussing the rôle of calcium in the etiology of tetany it is important to summarize the present status of our knowledge of calcium in the healthy organism.

To illustrate how minute is the amount of calcium involved in metabolic processes, one needs but consider that the soft tissues contain 0.01 per cent. of the calcium in the body, the remainder forming 7.7 per cent. of the skeleton; thus, a child weighing 10,000 gm. would only have 1 to 2 gm. in the soft parts.

The calcium content of the brain, according to Quest<sup>1</sup> is relatively high in early infancy, but diminishes as the child grows older, most rapidly in the first few months, then more slowly. In the fetus he found 0.168 per cent. calcium, in a new-born child 0.107 per cent., in a 4 months child 0.072 per cent., at 16 months 0.074 per cent., and at 2½ years there was 0.067 per cent. The nitrogen content was fairly constant, being 10 to 12 per cent. of the dried powder. In the brains of three infants dying with tetany 10, 11, and 12 months old, however, Quest found the calcium content distinctly diminished (0.041 per cent., 0.047 per cent., 0.0535 per cent.). Aschenheim<sup>2</sup> found the percentage diminished in two patients aged 7 and 10 months, and approximately normal in a third case (0.0373 per cent., 0.0234 per cent., 0.0557 per cent.). Leopold and von Reuss,<sup>3</sup> however, did not find any change from the normal in two infants 4 and 5 months old, respectively (0.062 and 0.038 per cent.). Michel Cohn<sup>4</sup> also found the calcium content of the brain in one case of tetany normal. In animals suffering from tetany parathyreopriva it has been demonstrated by MacCallum,<sup>5</sup> Pexa,<sup>6</sup> and Aschenheim<sup>2</sup> that the calcium of the brain is diminished. Cooke,<sup>7</sup> on the other hand, found a slight increased calcium content in the brains of dogs dying of tetany. However contradictory the results may appear,

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\*From the Chemical Laboratory of Cornell University Medical College.

1. Quest: *Jahrb. f. Kinderh.*, lxi, 114.

2. Aschenheim: *Monatschr. f. Kinderh.*, vii, 374.

3. Leopold and von Reuss: *Wien. klin. Wchnschr.*, 1908, No. 35.

4. Cohn, Michel: *Deutsch. med. Wchnschr.*, 1907, No. 48.

5. MacCallum and Voegtlin: *Jour. Exper. Med.*, 1909, p. 119.

6. Pexa: *Arch. f. Kinderh.*, 1910, No. 54.

7. Cooke: *Jour. Exper. Med.*, 1910, No. 12, p. 45.

they may be better interpreted in the researches of Loeb who showed that it is not the presence of one salt alone in the solution, but its interaction with other salts which influences nerve irritability. Either a diminution of the Na or an increase of the Ca diminishes the irritability. This is well illustrated by Aschenheim in his third tetany brain, in which, although the calcium content is high, the sodium also being high causes

Ca  
the quotient of the fraction  $\frac{\text{Ca}}{\text{Na}}$  — to equal 46, whereas in normal brains

it is only 19 to 26.

The application of calcium to the cerebral cortex has been shown by Sabbatani<sup>8</sup> to diminish its electrical excitability. Quest<sup>9</sup> was able by means of calcium-poor food to diminish the electrical excitability of the peripheral nerves in dogs, presumably by diminishing the calcium content of the nervous system. Stoeltzner<sup>10</sup> in an attempt to repeat this work, obtained contradictory results; and Pexa,<sup>6</sup> who fed puppies on a calcium-free diet, was unable to show any hyperexcitability of the peripheral nerves, although at autopsy the brains contained but one-fourth the normal amount of calcium. Rosenstern<sup>11</sup> attempted to attack this problem from the clinical side, and in cases of spasmophilic diathesis gave large doses of calcium chlorid (3 gm.) by means of which he was enabled to diminish the electrical excitability, the kathodal opening contraction rising within an hour to its maximum, the effect disappearing within twenty-four hours. Of twenty cases tested fifteen responded to the calcium and five were unaffected. To prove that it was the calcium and not the chlorid that was active, he used various other chlorid salts, but with them was unable to obtain results. Large doses of NaCl, on the other hand, increased the irritability. These influences on the electrical reactions have been investigated in the nerve-muscle preparation of the frog by Reiss<sup>12</sup> who showed that variations, i. e., a diminution in the calcium concentration of the solutions applied, could explain most of the electrical reactions of tetany with the exception of anodal closure.

An examination of the calcium content of the blood has also been carried out in order further to clear up the relationship of this substance to tetany. In parathyroidectomized dogs MacCallum and Voegtlin<sup>5</sup> found the amount diminished. Neurath,<sup>13</sup> using Wright's method, found that the calcium content of healthy children's blood was highest in early age and diminished as the child grew older, breast-fed children showing

8. Sabbatani: Quoted by Quest (see Note 9).

9. Quest: Wien. klin. Wchnschr., 1906, No. 27.

10. Stoeltzner: Neurol. Zentralbl., 1908, No. 2 (quoted by Escherich).

11. Rosenstern: Jahrb. f. Kinderh., ii, No. 2, p. 72.

12. Reiss: Ztschr. f. Kinderh., iii, No. 1.

13. Neurath: Ztschr. f. Kinderh., 1910, i.

a higher percentage than the artificially fed. Adding calcium to the food does not seem to increase the calcium in the blood. Parathyroidectomized animals also showed diminution of the blood-calcium. However, he emphasizes the fact that by Wright's method only ionic, i. e., precipitable calcium is estimated.

From the clinical standpoint this problem has been attacked by watching the therapeutic effect of doses of calcium in tetany. In post-operative tetany both in animals and man, large doses of calcium have been successfully used to relieve the symptoms. In the tetany of adults Curschmann and many others have had good results. In the infantile form Gerstenberger<sup>14</sup> got no results by the oral administration of calcium lactate, but his doses were only 2 gr. three times a day. Rosenstern<sup>11</sup> used it effectively by giving large doses. Intravenously calcium has yielded even better results.

At first sight it would seem that the most rational method of solving the whole problem would be by means of metabolism experiments; that is to say, ascertaining the total calcium intake and output. Although of undoubted value, this method has the disadvantage that it does not give any information as to the intermediate metabolism of the calcium, or as to how much calcium there is at any time available for the various parts of the body. It is surprising how little is known about the calcium metabolism, either in normal or in abnormal cases, and especially in cases of tetany.

The metabolism of normal breast babies has been better investigated on account of the ease with which it is possible to obtain a normal breast-fed child. Michel,<sup>15</sup> in a number of infants from 5 to 11 days old, found an absolute retention of calcium of about 0.2 mg., about 60 to 80 per cent. of the intake. In older children, aged 3 to 3½ months, Michel and Perret<sup>16</sup> and Schabad<sup>17</sup> have found slightly less retention, 150 to 200 mg., 40 to 50 per cent. of the intake. Langstein and Meyer<sup>18</sup> give as an average of various observations a retention in breast-fed babies of 176 mg. or 62.44 per cent. of the intake.

As far as bottle-fed babies are concerned, the figures vary from 1 to 5 per cent. retention (Cronheim and Muller<sup>19</sup>) to 44 per cent. Blauberg.<sup>20</sup> It must be added, however, that as Schabad remarks, the figures of Cronheim and Muller's cases are so low that they do not cover the calcium requirement of the organism. Langstein and Meyer give

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14. Gerstenberger: Jour. Exper. Med., Mar. 1, 1911.

15. Michel: L'Obstetrique, Mar. 15, 1896 (quoted by Schabad).

16. Michel and Perret: Bull. Soc. d'Obst., March, 1899.

17. Schabad: Arch. f. Kinderh., lii, 1-3, p. 68.

18. Langstein and Meyer: Säuglingsernährung und Säuglingsstoffwechsel.

19. Cronheim and Muller: Biochem. Ztschr., ix, 79.

20. Blauberg: Ztschr. f. Biol., xl, 19.

the average retention as 44.4 per cent. These figures must be regarded as more or less arbitrary, as not enough cases have been examined nor have the durations of the various experiments been of sufficient length.

#### CASE REPORT

In a case of tetany which we had the opportunity of observing, the calcium metabolism was studied in three periods of three days each. The history of the case is as follows:

*History.*—Female child 1 year old, non-instrumental delivery, breast-fed till the age of 10 months; apparently normal until 9 months of age (could stand and made attempts to walk alone), when it suddenly began to have convulsions, which were repeated. For this it was taken to a hospital and remained there two months. Two weeks after it left the hospital it came under our observation. Its condition was as follows:

*Physical Examination.*—A poorly developed anemic female child with very moderate rachitis, extremities held in typical tetany position, with marked spasticity. Eyes staring, face mask-like; Chvostek extremely marked; Trousseau present. Galvanic irritability showed kathodal opening contraction at 1.0 milliampere. Physical examination of the lungs, heart and other viscera was negative; temperature 102, pulse 120, respiration 30; stools dyspeptic; urine showed a faint trace of albumin.

On admission the child was put in a metabolism bed, and a four-day experiment carried out, the first day being disregarded. It was given in three days 2,300 c.c. of milk, containing by absolute analysis 2.5 per cent. fat, 2.25 per cent. protein and 6 per cent. sugar. During this time and for several weeks afterward the child ran a temperature up to 102. Physical examination including ears, urine, etc., failed to show the cause for this. The Pirquet test was negative.

During the following month the child's food consisted of little milk and plenty of cereal. During this period, although the child took its food badly and lost in weight, the symptoms of manifest tetany improved considerably, so that the child lost its fixed staring expression, Trousseau could no longer be obtained, the Chvostek became less marked and kathodal opening contraction had increased to 3 milliamperes.

May 25 the child was again put in the metabolism bed. It was fed on a cow's milk mixture (fat 3 per cent., protein 2.2 per cent., sugar 6 per cent.), of which it took 1,870 c.c. Its weight at this time was 12 pounds, 14 ounces. After four days the child was removed from the metabolism bed and put on a milk-free diet of soup and cereal for one week. Then it was given cod-liver oil 3i t. i. d., 10 ounces of milk a day, cereals, soup and bread and butter. The milk was then gradually increased. Under this regimen the symptoms rapidly improved, the temperature became normal, and remained so; kathodal opening contraction rising to 6 milliamperes, the only evidence of tetany being a slight Chvostek.

July 21 the third metabolism experiment was begun. During this the child received 2,250 c.c. milk, 120 gm. bread, 150 gm. rice, containing in all fat and protein as seen in the table. The child's weight at this time was again 14 pounds.

During the entire period of observation the stools were one to two a day, unformed, greenish-yellow, dyspeptic. The urine during the first few days of the illness contained a faint trace of albumin and a few hyaline casts. Subsequently the urine was normal.

#### SUMMARY

A child observed three months.

*Experiment 1.*—Manifest tetany; kathodal opening contracture 1 milliampere; fever; feeding raw cow's milk, calorically slightly insufficient.

*Experiment 2.*—Tetany markedly improved, kathodal opening contracture 3; fever; feeding raw cow's milk calorically insufficient through the child refusing nourishment.

*Experiment 3.*—After milk-free diet and cod-liver oil only symptom of tetany a slight Chvostek; kathodal opening contraction 6 milliamperes.

From Table 1 of the balances in these three experiments, it will be seen that although the child was fed a calorically insufficient mixture, the nitrogen balances were positive, 50 per cent. in the first experiment, and 38 per cent. in the second.

TABLE 1.—FAT AND NITROGEN IN AN INFANT WITH TETANY

Experi- ment	—Fatty Acids, K. and S.—				Total Nitrogen					
	Intake, gm.	Feces, gm.	Resorption,		Intake, gm.	Urine and Feces, gm.	Retention,		Resorption,	
			gm.	Per cent.			Per cent.	gm.	gm.	Per cent.
1 ...	50.46	5.72	44.7	88.7	8.13	4.06	4.07	50.0	7.71	88.2
2 ...	44.8	1.46	43.34	96.7	6.73	4.12	2.61	38.7	5.25	78.0
3 ...	93.6	4.8	88.8	94.8	14.32	7.14	7.185	50.0	13.64	95.2

The fat balance obtained by the method of Kumagawa and Suto, showed an intake of 54 gm. in Experiment 1, with resorption of 88 per cent.; the resorption in the second being much better (96 per cent.); in the third about 95 per cent., showing an improvement in the fat resorption in the last two experiments.

TABLE 2.—CALCIUM OXID BALANCE

Experiment Duration, Days,	Food						— Urine —		— Feces —		Resorption		Retention			
	Amt., c.c.	Composition				Intake, CaO, gm.	Amount c.c.	CaO, gm.	Amt., gm.	CaO, gm.	Absolute, gm.	Per cent.	Absolute, gm.	Per cent.		
		2.5	F.	2.2	P.										6	S
1 3	2,300	2.5	F.	2.2	P.	6	S	2.921	635	0.0314	20.0	1.7834	1.376	38.9	1.1062	37.8
2 3	1,870	3	F.	2.2	P.	6	S	2.917	295	0.0288	7.0	0.8044	2.1128	72.4	2.084	71.3
3 3			Milk,	Rice,	Bread			3.918	1,026	0.220	16.0	1.426	2.492	63.6	2.272	58.7

The calcium metabolism as seen from Table 2 shows that in Experiment 1, with an intake of 2.9 gm. of calcium, there was an absolute resorption of 1.376 gm., or 38 per cent., and an absolute retention of 1.1062 gm. or 37.8 per cent. In the second experiment with practically the same intake there was only 0.8 gm. excreted in the feces, an absolute resorption of over 2.0 gm. or 76 per cent. and a retention of 71 per cent. The amount of calcium excreted in the urine in both of these experiments was about the same. In the third experiment, in which the intake was increased by 1 gm. of calcium, the amount of dried feces being almost the same as in Experiment 1 (16 gm. as compared with 20 gm.), the actual excretion was less than in Experiment 1, the absolute resorption

was 2.4 gm. as compared with 1.3 gm. in Experiment 1, and 2.1 gm. in Experiment 2, the percentage being 63 per cent., almost as large as in Experiment 2 and almost twice as large as in Experiment 1. The retention was 58 per cent. The amount of calcium oxalate in the urine of Experiment 3 is high, due to the unfortunate admixture of some of the feces. However, even if we assume that all the calcium found in this urine in Experiment 3 was derived from this contamination, nevertheless, by adding this to the calcium of the feces we still find the excretion less than in Experiment 1, although the child was getting 1 gm. more calcium by mouth.

It has been shown that the calcium output may be increased by fever,<sup>21</sup> and it might be argued that the comparatively low retention (37 per cent.) in our first experiment was due to this cause; however, during the second experiment the child ran a similar temperature and the retention had almost doubled.

Concerning the rickets, Schabad<sup>22</sup> has shown that as the rickets improves the calcium retention is bettered. In our case it seems hardly probable that the rickets was much of a factor, for the child had no enlargement of the epiphyses, had been able to stand, and had made attempts at walking at 9 months; in fact, the rosary was the only symptom. In a period of five weeks, during which time there had been no especial therapy or diet instituted for rickets (cod-liver oil was given only after the second experiment) and the child having lost weight, the improvement in the calcium retention could scarcely be attributed to improvement in the rickets.

The only cases comparable to ours are that of Cybulski<sup>23</sup> and those of Schabad.<sup>24</sup>

Cybulski's case was an infant 7 months old weighing 6,100 gm. (13.4 pounds). It was supposedly a non-rachitic infant suffering from manifest tetany. Cybulski did metabolism experiments of three periods of three, three, and four days each. The child received cow's milk in the first and woman's milk in the second and third experiments. From the figures in Table 3 it will be seen that there is a progressive improvement in the calcium retention, the figures showing first 20.8 per cent. retention, then 53.7 per cent., and last 87.2 per cent. The fat resorption, as in our experiment, also improved, but the nitrogen during the first experiment was negative.

The gradual increase in the amount of calcium retained might well be ascribed to the fact that the child received woman's milk, for this in itself ordinarily causes an increase in the calcium retention. Further-

21. Schkarin: *Arch. f. Kinderh.*, 1905, xli.

22. Schabad: *Arch. f. Kinderh.*, liv, Nos. 1-3.

23. Cybulski: *Monatschr. f. Kinderh.*, November, 1906, p. 409.

24. Schabad: *Monatschr. f. Kinderh.*, ix, No. 1.

more, the child during the first experiment was not in nitrogen equilibrium; moreover, it is very improbable that a child of the proletariat weighing only 13.4 pounds at 7 seven months should be free from rickets. In addition, Schabad calls attention to the absence of spastic extremities and the Trousseau sign, doubting as to whether the case is really one of tetany. It seems to us, however, that the electrical reactions undoubtedly classify the case as tetany, and it would seem more than likely that the convulsions could be ascribed to this cause.

TABLE 3.—CYBULSKI'S CASE. CALCIUM OXID BALANCE

Experi- ment No.	Dura- tion, Days	Intake CaO, gm.	Urine CaO, gm.	Feces CaO, gm.	Resorption Absolute, gm.	Per cent.	Retention Absolute, gm.	Per cent.
1. ...	3	1.756	0.0074	1.382	....	21.4	0.366	20.8
2. ...	3	0.997	0.0089	0.453	....	54.7	0.536	53.7
3. ...	4	1.531	0.031	0.1650	....	89.3	1.353	87.2

Schabad describes two cases of rickets complicated by tetany,  $2\frac{1}{2}$  and 3 years old, respectively, in which the calcium retention had sunk to 4 per cent. in the one and 15 per cent. in the other. By the administration of cod-liver oil and phosphorus he was able to raise the retention in the second case from 15 per cent. to 76.6 per cent., and coincidentally noted the diminution in the electrical excitability—the kathodal opening contraction going from 2 to 6 milliamperes and the Chvostek and laryngo-spasm disappearing. It is difficult to compare these cases with ours, first, on account of the difference in ages, second, their marked rachitis and, third, the fact that Schabad's metabolism experiments did not include the stage of manifest tetany. It is seen that in his cases also the increase in the calcium retention and the improvement in the symptoms go hand in hand.

TABLE 4.—NITROGEN FRACTIONS IN URINE IN THE AUTHOR'S CASE OF TETANY

Date	Amt. c.c.	Sp. Gr.	Total Nitrogen, gm.	Urea, gm.	Urea N Per cent. Total N	NH <sub>4</sub> Ni- trogen, gm.	NH <sub>4</sub> N Per cent. Total N
....	....	....	....	....	....	....	....
....	....	....	....	....	....	....	....
....	....	....	....	....	....	....	....
April 18-19 .....	130	1010	1.07	0.69	64.5	0.0585	5.47
April 19-20 .....	205	1016	1.06	0.73	68.8	0.051	4.81
April 20-21 .....	300	1010	1.08	0.84	77.8	0.072	6.66
May 25-26 .....	95	1020	0.930	lost	....	0.04	4.3
May 26-27 .....	65	1025	0.740	0.54	73.0	0.044	5.40
May 27-28 .....	135	1012	0.970	0.607	62.6	0.091	9.39
July 19-20 .....	380	1009	2.542	2.086	82.0	0.234	9.21

Haskins and Gerstenberger<sup>25</sup> in a child suffering from manifest tetany (negress 14 months old) found the calcium retention 11.7 per cent. Eight months later, after treatment, with the child apparently greatly improved, the calcium retention was 12.8 per cent.

25. Haskins and Gerstenberger: Jour. Exper. Med., March, 1911.

## CONCLUSIONS

From the foregoing review of the subject, and analysis of our case, one might conclude as follows:

1. Sufficient data are not available to state definitely the absolute and percentual figures for calcium retention in the normal child.
2. The calcium in our case, as compared with the few normal cases on record, does not seem diminished.
3. From Cybulski's and our cases it appears that the calcium retention improves as the tetany disappears.

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## REPORT OF BRAIN CASES

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During the past year a number of interesting cases involving the nervous system occurred in the service of my colleagues and myself at the Cook County Hospital, a few of which I herewith report.

**CASE 1.**—Johanna W., aged 8, of German parentage, but born in France. She was brought to the United States when 3 years old. No serious illness had occurred during the first few years of life. At the age of 6 she started to school, which she had to give up shortly thereafter on account of headaches. At that time the father noticed some change in the right eye and later a similar change in the left eye. The affection was of such a nature that she could see better in a dim light. She was treated with but little success for several months. The sight thereafter gradually improved and her headaches were relieved to the extent that she was again able to attend school. About a year ago the headaches returned and were very severe. Sleep was much disturbed and the only comfortable position when in bed was with the head lower than the trunk. She had not vomited before entering the hospital. Several months ago she had measles. This seemed to aggravate her condition. It was noticed about this time that she used her arms awkwardly, stumbled in walking, and had difficulty in talking. While out walking on one occasion she stumbled and fell. The injury did not seem severe, but immediately following the fall she had a slight convulsion which was not accompanied by unconsciousness. Her symptoms gradually grew worse. Walking became more difficult, her speech less distinct and she seemed to have some trouble in swallowing. She was brought to the County Hospital October 3, 1910, and walked into the examining room.

**Family History.**—Father and mother healthy. No history of syphilis. This was the only child.

**Examination.**—The patient was a girl of average height for her age, but undernourished; no tenderness of head nor rigidity of neck; face rather expressionless, mouth open; throat negative; no cervical adenitis; chest symmetrical and well formed.

**Lungs:** Percussion negative, auscultation negative.

**Heart:** Area not increased, tones normal, no murmurs.

**Abdomen:** Liver and spleen not enlarged. Abdomen otherwise negative.

**Extremities:** No edema or eruption.

**Nervous System:** Mentally clear, but unable to speak distinctly. Later she was able to answer questions only by nods and shakes of the head.

**Muscular System (motor power):** No absolute paralysis, but paresis. The left abducens was paretic; slight horizontal nystagmus.

**Face:** She moved only the left side of the face and that but little; could not protrude tongue nor corrugate lips; opens mouth; palatal reflex present but patient could not be induced to raise palate voluntarily.

**Arms:** Marked spastic paresis of left arm which was held in extension; slight spastic paresis of right arm.

**Legs:** Held in strong extension; partial flexion was possible but was never maintained; marked spasticity; the left was much more involved than the right.

**Trunk:** When placed in sitting posture patient had difficulty in maintaining her position. The spine showed scoliosis which was easily corrected.

Reflexes: Arm-jerks active, knee-jerks exaggerated. Babinski present on both sides. Oppenheim present. Gordon not elicited. No ankle or patellar clonus obtained.

Sensation: Touch intact; pain, analgesia of left side; temperature, intact; muscle sense intact; coordinated movements not well performed; patient had to be fed, but the difficulty seemed to arise from stiffness and weakness primarily. Taste and hearing so far as tested were all right.

Examination of left eye showed a retinitis.

Spinal puncture was made several days after admission to hospital. Pressure not increased; fluid clear. Prolonged centrifuging revealed very few polynuclear cells and lymphocytes and no bacteria.

Pirquet skin reaction was made and found negative.

Wassermann examination of blood was negative. No leukocytosis. Urinalysis was negative.

*Subsequent Course.*—In the subsequent course of the disease all symptoms became more pronounced and the patient passed into a state of profound coma, which continued for a few weeks before death, which occurred Dec. 27, 1910. She had in this period, several times a day, a slight general convulsion, during which the whole body would become rigid and the face flushed. Nasal feeding was necessary for several weeks. Decubitus developed on dependent parts of the body. The pulse was accelerated during her stay in the hospital, and she had at times a rise in temperature. The respiratory rhythm was disturbed during the period of coma.

*Diagnosis.*—In view of the general symptoms of cerebral pressure, namely headaches, retinitis, later vomiting and increasing unconsciousness, and in view of the focal symptoms, especially the paralysis of the right facial and the marked spastic paresis of the left arm and leg, in contrast to the slighter paresis of the right arm and leg and left facial, also the dysarthria and dysphagia, the diagnosis of a brain tumor located in the pons was made. In investigating the etiology of the tumor, it was found that the blood was negative to the lues reaction, and that she gave a negative skin tuberculin reaction. While this latter point could not be decisive against tuberculosis, a negative reaction might be of greater value in a diagnostic sense than a positive reaction. Consequently it was thought that the tumor was a glioma, or might prove to be a solitary tubercle.

*Necropsy.*—The postmortem was made by Dr. Boughton, whose diagnosis was as follows: 1. Glioma of pons. 2. Decubitus on both trochanters, right ilium, sacrum and external maleolus. 3. Parenchymatous degeneration and slight passive congestion of the liver. 4. Fatty degeneration of the kidneys.

It will be noted from the history of this case that fully two years before death symptoms of brain tumor started. The process had evidently existed for some time before distinctive localizing symptoms developed themselves. The importance of recognizing brain tumors early is self evident. If we can satisfy ourselves that they are not luetic, and to this end I would not depend on a negative Wassermann but also resort to antiluetic treatment, there is only one course of treatment open, and that is operation, first for the symptomatic relief, and second, if possible, for the removal of the growth.

CASE 2.—Wanda M., aged 8½ years, admitted to the hospital Nov. 16, 1910; of German parentage but born in South Africa. Three weeks before admission the child began to feel somewhat indisposed, did not care to go to school, lost her appetite, complained of headache, was feverish and vomited twice or three

times. The mother insisted on the child continuing in school for about three days following her first complaints. The headache grew worse and she was taken from school, with all symptoms continuing and exaggerated. In the course of a few days she began to tremble in the legs and arms. This was mild in character until about five days before entering the hospital, when the child began to tremble all over. She complained of stiff neck and back and said she had pain everywhere, but especially in the head, shoulders and arms.

*Previous History.*—Had had measles and small-pox.

*Family History.*—Negative. There was one other child who was healthy.

*Examination.*—The patient was a fairly well nourished girl of 8 years; the skin was pale and her expression was anxious. She breathed with the mouth partially open. She seemed to be in great pain, was restless and irritable. Every few minutes the pain was so great that she went into a semi-clonic condition all over the body and then cried out loudly, a sharp rasping cry, then quieted a little; the same thing was repeated in a short time. Her mind was clear. There was no defect of speech.

*Head:* The head was not enlarged and there was no evidence of injury about the scalp. The eyes were wide open. The pupils were dilated but reacted to light. There was no discharge from the eyes or nose. There was sordes on the teeth.

*Neck:* A few postauricular glands were palpable on the left side. The neck was rigid. When the head was raised the shoulders and trunk came up also.

*Thorax:* There was good resonance over the lungs on both sides and the boundaries were normal and mobile. A few moist rales were heard posteriorly.

*Heart:* Area and sounds normal; no murmurs or adventitious sounds.

*Pulse:* Soft, easily compressible, and accelerated.

*Abdomen:* Liver and spleen not palpable, no abdominal tenderness.

*Genitalia:* Negative. No enlargement of glands except as above noted.

*Extremities:* The arms were held in semiflexed position all the time and were kept in chronic clonic motion. The fingers could be flexed and the arms extended, adducted, and abducted, but the child complained of considerable pain whenever they were moved. The back was held rigid. The lower extremities were held in semiflexion. A decided Kernig was present on both sides.

*Reflexes:* Eyes reacted to light and accommodation. Knee- and Achilles-jerks somewhat exaggerated. Reflexes of upper extremity present.

*Blood examination:* Reds, 4,900,000; whites, 11,000; hemoglobin, 95 per cent.; index, 0.9.

*Differential:* Small mononuclears, 13; large mononuclears, 7; polynuclears, 80.

*Spinal fluid:* Examined Nov. 17, 1910. Amount, 16 c.c., under pressure; looked like water; centrifuged nine hours; a few lymphocytes but no bacteria found.

*Urine,* negative.

*Wassermann reaction,* negative.

The temperature on entering the hospital was 100.4 F. rectal; pulse 120.

Following spinal puncture the pulse-rate dropped to 90, to 80, and the rectal temperature remained below 100 F. All symptoms subsided, and in a few days the patient was convalescent.

*Diagnosis.*—The severe headaches, the rigid neck and back and the presence of Kernig's sign were sufficient to suggest meningeal involvement. She had a general tremor involving the head, trunk and extremities. The tremor was constant. It was greatly increased in voluntary movement or in touching the patient, as she was hyperesthetic. The tremor was coarse, the excursions being large. During movement of the patient the term semi-clonic would better describe it than tremor.

In regard to the lumbar fluid, the stained specimens made after centrifuging the fluid nine hours failed to reveal any organisms, and only a few lymphocytes. This might have been interpreted as a negative finding, or one suggesting a

tuberculous or luetic infection. A Wassermann reaction of the patient's blood was negative; consequently lues was strongly improbable.

The patient recovered rapidly following the lumbar puncture, so that tuberculosis could not be considered. There was no infection of the nose, throat, ears or sinuses that could be made out and to which the meningeal symptoms might have been considered secondary. She had what looked like a small burn over the left elbow, but there was no evidence of any considerable infection of it. There was no relation to be made out between this and the meningeal involvement. There had been no injury to the head nor was any intoxicant or narcotic to be considered in the matter.

After being in the hospital several days an examination of a vaginal smear showed it positive for gonococci. She was, therefore, transferred to the children's annex.

While we might speculate on the character of the meningeal involvement, we certainly had no definite point on which to make an etiologic diagnosis, directly or indirectly. It might be consistent for us to consider the possibility of serous meningitis, because she presented some of the symptoms of meningitis, because the lumbar fluid was under pressure, because it was practically negative on examination, and because she recovered promptly following puncture. It possibly had some toxic or infectious origin, a view which might be reinforced by the existence of a slight temperature, but we had no leading points on which to base it nor with which to associate it.

CASE 3.—M. L., girl aged 13, Jewish, born in Russia.

*Family History.*—This was the oldest and only living child. The mother's second pregnancy terminated in a miscarriage at the third month. The third child born was healthy at birth but died at six months of summer complaint. The result of the fourth pregnancy was a dead-born child. No insanity on the father's or mother's side so far as known. Parents were both in good health.

*Personal History.*—Her early development in regard to walking and talking proceeded about the same as most children. She was bright and as quiet as the average child. The patient had brain fever when 2½ years old and was sick for three months. At six years she had scarlet fever, but recovered entirely. She never seemed to care much for the company of children, preferring to be with older people. She started to school at 8 years but did not learn well.

Last summer (1910) the patient was attacked by four children, who threw her down and beat her. Her cries brought a neighbor, who found her greatly frightened, crying and trembling all over. When the mother returned home in the evening she was still greatly agitated. That night she slept but was very restless. On the following day, Tuesday, she went with other children for a boat ride. On returning home the mother thought she appeared sad. She answered questions and talked voluntarily. Wednesday evening, when getting out of the bath tub, she fell and struck her head. The mother noticed on helping her up that she was very pale, but she complained but little of her head hurting. When the mother returned from her work Thursday she found the patient crying. She said she did not want to live, because the children annoyed her. That night she slept but little, cried a great deal and talked in this same strain.

On the following day she stopped talking and maintained silence for ten days. She would not leave the house, would seldom answer a question, and if so, with a grunt, and would not eat unless her mother insisted on it. At the end of ten days she suddenly became very talkative and noisy; she talked in a rambling

way and would repeat almost everything that had been said to her during her quiet spell. She wanted to go to parks, nickel shows, etc., and wanted to become an actress.

Then periods of complete silence and agitation alternated regularly every ten days, for six months. She was taken to a sanatorium, from which she escaped after four weeks. She did not appear to improve while there, but after returning home there was a period of three months in which she seemed to do much better, did not have her mute spells and was quieter in general. While in the sanatorium it was noticed that the spells of silence and agitation were not so uniform. At no time had she had delusions or hallucinations.

Following the three months improvement, the mother noticed one day while the child was at the piano that a change came over her. She stopped playing and looked strange. On the mother inquiring the cause of the change she said her head hurt. After awakening on the following morning she did not speak for thirteen days. During this time she started to menstruate for the first time. Following a similar alternating period of agitation, she became quiet and during this time she also menstruated. She was subsequently removed to the Elgin Asylum.

*Examination.*—Lungs, heart and abdomen negative; urine negative.

*Nervous System:* Head did not show any evidence of past injury. Eyes reacted to light and accommodation.

*Muscular System:* No paresis or paralysis.

*Sensation:* No disturbance detectable.

*Reflexes:* Present but not exaggerated. No hysterical stigmata could be made out.

The family history was strongly suggestive of lues. The girl, however, did not present any evidence of luetic lesions past or present.

The mental change followed closely on the fright and head injury. The alternating periods of silence and agitation followed each other with great regularity. She showed a remarkable memory during her periods of agitation, not only of what was said during her spells of silence, but of early events in her life, of her native city, Odessa, etc. She was also physically restless at these times, while in her periods of silence she would stand in one position for hours.

In view of the clinical history of this case the question of diagnosis would probably consider circular insanity and dementia præcox. The alternating character of the periods of depression and emotional excitement would strongly suggest a circular form of insanity. However, such a picture might occur in the early stage of dementia præcox.

During her periods of depression, there seemed to be a complete suspension of mental activity, lack of interest in her surroundings and no tendency to physical effort, all of which points are strongly suggestive of dementia præcox. At no time, however, had she had the hallucinations or delusions that are frequently present in the beginning of dementia præcox.

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## SPLENOMEGALY (GAUCHER)

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It is the object of this paper to report the history of a family, several members of which suffer from a type of splenic enlargement usually designated as that of Gaucher, and to make a critical study of all the reported cases of this disease, with the hope of proving that although these cases resemble other diseases, yet closer study gives overwhelming proof that they must be classed by themselves as an entirely distinct and separate disease. The diseases from which it is especially to be differentiated are splenic anemia in adults and von Jaksch's disease in infants. Under the term "splenic anemia," Osler includes all those cases of idiopathic enlargement of the spleen associated with anemia, which were formerly classified as splenic pseudoleukemia, anemia splenica, lymph adénie splénique and splenic form of Hodgkin's disease. He states: "I purposely have not spoken of anemia with enlarged spleen in very young children, a subject which requires separate consideration."

The entity of splenic anemia is not at all granted. Stengel in his paper on "Splenic Anemia" says: "I have elsewhere expressed doubt regarding the individuality of such a condition and the conviction that many different sorts of diseases have been classed under this term."

### REPORT OF CASES

*Family History.*—Father and mother both living and well; there is no tuberculosis in the family; nor could any luetic history be obtained. The mother has given birth to four children, and has had no miscarriages nor stillbirths. Anna, the oldest child, is 11 years old. Lilly died in 1909 at the age of 8; Freda is 9 years old, and Max, the youngest, is 4 years old. Wassermann reaction of mother negative.

The boy came to my notice at the Vanderbilt Clinic June 10, 1911 (in the service of Dr. C. Herrman) where he was brought for treatment on account of a progressive enlargement of his abdomen. The mother stated that an older child (Lilly) had had a similar condition and that that child died two years previously; as this child (Lilly) had been at Mt. Sinai Hospital (1906) at a time when I was a member of the house staff of this hospital, I can recall the case very clearly. At the hospital no diagnosis was made. This child was also treated at the Vanderbilt Clinic in 1904, and notes of the case show that at that time the child had a much enlarged spleen and liver. No diagnosis was made at the time.

**CASE 1.**—Anna: Physical examination of this child revealed nothing abnormal; she was in good physical condition, the liver and spleen were not enlarged.

**CASE 2.**—Lilly: This child died two years previously at the age of 8; she had measles at 2 years; no other diseases of infancy; no history of malaria. At 4 years the child began to be troubled with enlargement of the abdomen; also complained of dragging sensation in the side and weakness. The abdomen was progres-

sively increasing in size; at the time the child was at the hospital the liver was 10 cm. below the free border of the ribs, and the spleen was beyond the median line and well filled the left iliac cavity. The child had at no time any hemorrhages nor oozing from the gums, and there was no discoloration of the face.

The blood examination showed the following:

Red blood-cells, 3,440,000; white blood-cells, 6,200; hemoglobin, 68 per cent.; differential count, normal; no abnormal cells present.

Mixed treatment, arsenic and  $\alpha$ -ray, were ineffectual and the child was discharged from the hospital unimproved. A few months later the child suddenly developed dyspnea and cyanosis and succumbed before a physician could be called (Fig. 1).

CASE 3.—Freda: The third child was 9 years old; she had no diseases of infancy, and there was no history of malarial infection. During the last year she complained of pain in the abdomen. Physical examination showed the liver to be enlarged; the edge was palpable 2 inches below the free border of the ribs. The spleen was not enlarged and the edge was not palpable. The blood examination

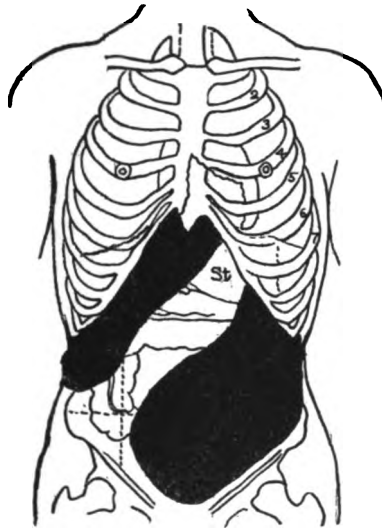


Fig. 1.—Enlargement of liver and spleen in Lilly, Case 2.

showed the following: Red blood-cells, 4,344,000; white blood-cells, 7,000; hemoglobin, 75 per cent.; differential count, normal; no abnormal cells present.

There was no pigmentation of the skin, and no history of any hemorrhages nor oozing from the gums or lips; there was no bone tenderness and the lymph-glands were not enlarged. Whether Freda was suffering from the same disease as Lilly and Max (the latter case to be described later) only the future will reveal; but she had a much enlarged liver which cannot be attributed to any other cause; whether she will develop a large spleen later cannot be definitely stated (Fig. 2).

CASE 4.—Max: The fourth child was a boy 4 years old; he had no diseases of infancy; he was not rachitic, and there was no history of malarial infection. About one year previously he was thrown down by a horse; at this time the attending physician told the mother that the child had a large liver and spleen; since that time the mother noted a progressive enlargement of the abdomen and brought the child to the clinic on that account. Examination of this child showed there was a distinct discoloration of the face; the color varied from light yellow to golden hue. The pigmentation was most marked at the bridge of the nose and around the eyes. There was no discoloration of the conjunctivæ. There was a

general languid appearance, and the child moved about very slowly; the child did not complain of any pain nor was any tenderness to be elicited in the chest or abdomen. Heart and lungs were normal. The liver was much enlarged and the edge was palpable at the umbilicus; there was no tenderness over the liver. The spleen reached to 2 inches below the umbilicus and extended over the median line to the right as far as the mammary line.

The blood examination showed the following: Red blood-cells, 2,208,000; white blood-cells, 5,000; hemoglobin, 35 per cent; differential count, normal; no abnormal cells found. There was no history of hemorrhages; no bone tenderness, and the lymph-glands were not enlarged (Fig. 3). Wassermann reaction negative.

It is my object now to epitomize all the cases reported in the literature and to try to make a critical study, with the hope of collecting data to show that they have much in common, and that they differ greatly from other similar diseases, and that, in fact, "Splénomegaly (Gaucher)" is an entity.

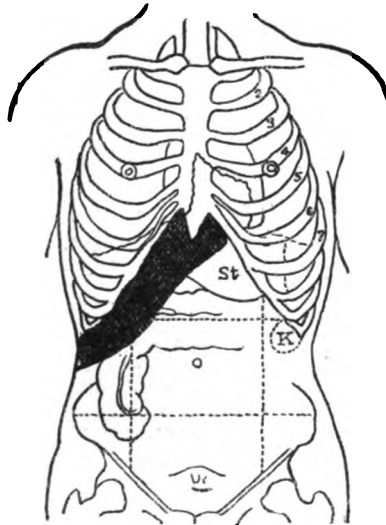


Fig. 2.—Enlargement of liver in Freda, Case 3.

**GAUCHER'S CASE.<sup>1</sup>**—Female, aged 32, died of intercurrent pulmonary tuberculosis; splenic enlargement since 7 years old, accompanied by enormous enlargement of liver; repeated epistaxis; ulceration and oozing of blood from the gums. The blood showed simple anemia. Necropsy showed tuberculosis of lungs and peritoneum, moderate enlargement of liver, large spleen (4,770 gm.); lymph-nodes normal.

**PICON AND RAMOND'S CASE.<sup>2</sup>**—Female, aged 32, with a history of menorrhagia, abdominal pain, swollen and bleeding gums; operated on for suspected fibroid uterus; large spleen found; spleen was removed; patient recovered from operation. The blood showed simple anemia; spleen weighed 2,800 gr. Four years previous to operation there was a history of trauma to abdomen.

1. Gaucher: Thèse de Doctorat-Splénomégaly Primitif; Epithélioma primitif, de la rate, 1882.

2. Picon and Ramond: Hypertrophie de la rate, Arch. de méd. exper. et Anat. Path., 1896.



**COLLIER'S CASE 1.**<sup>3</sup>—The spleen was taken from the body of a female child aged 6 years, who was admitted to Radcliffe Infirmary April 4, 1894, and died there Sept. 7, 1894. The mother stated that the child was healthy up to 8 months, when she had a severe illness the nature of which is not known. When 2 years old the abdomen was noticed to be enlarged, and was steadily increasing in size. The blood was examined, but no excess of white blood corpuscles was found. The red blood corpuscles were misshapen and did not form good rouleaux. Slight bending of ribs, but no other signs of rickets, was present. Death seemed to be accelerated by an attack of "epistaxis and sickness." The mother stated that she had seven children, four of whom died previously to this one—one of inflammation of the lungs, two of consumption of the bowel and one in the infirmary six years previously.

Necropsy showed no tuberculosis; spleen weighed 4 pounds 2 ounces; child 23 pounds; all mesenteric glands enlarged.

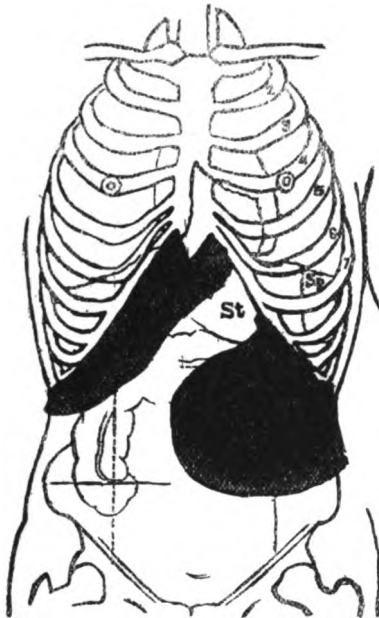


Fig. 3.—Enlargement of spleen and liver in Max, Case 4.

**COLLIER'S CASE 2.**—The sister died at an infirmary Nov. 27, 1888; was admitted with bronchitis and enlarged spleen; gradually lost strength and died of exhaustion. No tuberculosis was found on necropsy. The spleen was found to be enormously and uniformly enlarged; weight 25 ounces. On section it was found congested and its substance was firm though somewhat friable. (Reported Jan. 16, 1895.)

**WEICHSSELBAUM'S CASE.**<sup>4</sup>—Male, aged 21, soldier; no history given; spleen removed by operation.

3. Collier: A Case of Enlarged Spleen in a Child Aged 6, Tr. London Path. Soc., 1895.

4. Weichselbaum: Primar multiple Endothelsarkom der Milz, Virchows Arch. f. path. Anat., 1881.

BOVAIRD'S CASE 1.<sup>5</sup>—Female, aged 3; father and mother living and well; nine children; one stillbirth at eight months; four died during infancy from summer complaint; five are living; no previous diseases.

For about one year the mother noted enlargement of abdomen, steadily increasing; also noted a mass on right side of abdomen as well as on left; was sent to hospital; the child was of normal stature, well nourished, not anemic; skin dusky; some signs in the lungs; liver dulness from fourth space to 3 inches below free edge of ribs; edge was hard and sharp; spleen extended to within  $\frac{1}{2}$  inch of median line at umbilicus; lower end on a level with anterior superior spines of ilium; edge sharp and hard; nodes in each axilla; one node the size of a bean; both sets of inguinal glands were slightly enlarged, not tender, freely movable. Blood, 4,400,000 reds, 9,000 whites, hemoglobin 75 per cent.

TABLE GIVING ANALYSIS OF

Author	Case No.	Sex	Age	First Splenic Enlargement Noted at Age of	Time Under Observation, Years,	Spleen Enlarged	Liver Enlarged	Lymph-Nodes	Red Blood Corpuscles	White Blood Corpuscles
Gaucher .....	1	F	32	7	25	Much	Much	Normal	Simple Anemia	
Picon and Ramond ..	2	F	32	?	?	Much	?	?	Simple Anemia	
Collier .....	3	F	6	2	4	Much	?	?	R.B.C misshapen	
									No excess of W.B.C.	
Collier .....	4	F	10	?	?	Much	?	?	?	?
Weichselbaum ...	5	M	21	?	?	Much	?	?	?	?
Bovaird .....	6	F	3	3	3	Much	Much	Enlarged	4,400,000	9,000
Bovaird .....	7	F	13	3	13	Much	Yes	Enlarged	2,880,000	4,000
Brill .....	8	M	9	?	?	Much	?	?	?	?
Brill .....	9*	M	31	15	19	Much	Much	Normal	3,200,000	8,240
Brill .....	10	F	34	19	19	Much	Much	Normal	4,800,000	7,168
Schlagenhaufen ...	11	F	41	5	36	Much	Slightly	Normal	4,700,000	1,300
Schlagenhaufen ...	12	F	33	20	13	Much	Slightly	Normal	5,735,000	3,435
Marchand .....	13	F	?	?	20	Much	Much	Normal	No leukocytosis	
Reuben .....	14	F	8	4	4	Much	Much	Normal	3,440,000	6,200
Reuben .....	15	F	9	—	1	None	Much	Normal	4,340,000	7,000
Reuben .....	16	M	4	4	1	Much	Much	Normal	2,208,000	5,000

\*Ascites present. No jaundice in any case.

The child was in the hospital from Nov. 28, 1896, to Dec. 22, 1896; seemed quite well; chest signs cleared up; gained  $1\frac{1}{4}$  pounds. Treatment, Fowler's solution.

Some time prior to July 26, 1899, the child had been failing; nose bled frequently and quite severely; lost flesh; face and hands had become bronzed. At this time—age 6 years—across the bridge of the nose and on the cheeks and hands there was diffuse bronzing of the skin; abdomen spare, prominent; superficial veins enlarged; liver extended from sixth rib to within  $1\frac{1}{2}$  inches of umbilical line. The spleen later extended into and filled the right iliac fossa. The glands, inguinal, cervical and axillary, were slightly enlarged. Blood, 4,180,000 reds, 14,000 whites, Hgb. 62 per cent. In December, 1899, the child had not improved but was able to attend school.

5. Bovaird: Primary Splenomegaly—Endothelial Hyperplasia of the Spleen—Two Cases in Children; Autopsy and Morphological Examination in One, *Am. Jour. Med. Sc.*, 1900.

BOVAIRD'S CASE 2.—Female, sister of above patient, aged 13, had measles at 5 years; at 7 an eruption on the scalp. At the age of 3 the mother noticed an enlargement of the abdomen which progressively increased in size, and also pigmentation of the skin, especially across the nose. The child complained of a little discomfort from the enlarged abdomen and was a little short of breath. When admitted to the hospital she was small in stature for her years, fairly well nourished, skin dusky; across the nose, underneath the eyes and on the upper lip there was a decided brownish pigment. Liver dulness extended from the fifth space to the margin of the ribs; edge could not be felt; superficial veins were dilated. The spleen extended to 1 inch above the umbilicus, passed obliquely to the anterior superior spines and was hard and smooth. There was slight enlargement of right inguinal nodes, moderate enlargement of both submaxillary and one pal-

## CASES OF SPLENOMEGALY (GAUCHER)

Pigmentation	Location of Pigmentation	Hemorrhages	Splenectomy	Autopsy	Still Living	Weight of Spleen, gm.
?	?	Epistaxis, bleeding gums	..	+	..	4,770
?	?	Menorrhagia, bleeding gums	+	..	..	2,800
?	?	?	..	+	..	2,070
?	?	?	..	+	..	880
?	?	?	+	..	..	....
Bronzed	Face, nose, hands	Epistaxis	..	..	+	....
Brownish	Nose, face	?	+	+	..	6,200
?	?	?	..	..	..	....
Light Yellow	Face, hand, neck	Epistaxis	..	+	..	5,280
Brown-Yellow	Face, hand	Epistaxis, oozing gums	..	+	..	7,000
Brown	Face, lower extremity	Gums epistaxis	..	+	..	3,510
Bronzed	Cheeks, forehead	Epistaxis	..	..	+	....
Icteric-Brownish	?	?	..	+	..	2,720
Roman Gold	Face	—	..	..	..	....
.....	.....	—	..	..	+	....
Roman Gold	Face, hands	Epistaxis	..	..	+	....

pable node in each axilla; no enlargement of the epitrochlear nodes. Blood, 2,880,000 reds, 4,000 whites, Hgb. 60 per cent. Mixed treatment was tried without effect. Three years later the condition was the same; the child did not grow in stature nor gain weight. Readmitted to the hospital in 1899, aged 16 years. The patient was fairly well nourished, face and hands deeply bronzed; liver dulness began at the sixth rib; edge  $1\frac{1}{2}$  inches below the free costal margin; the spleen filled the whole of the left iliac fossa. Blood, 3,550,000 reds, 7,000 whites, Hgb. ? Splenectomy was performed May 17, 1899, by Dr. A. J. McCosh. The patient died three hours after operation. The spleen weighed  $12\frac{1}{2}$  pounds.

BRILL'S CASES.—Father and mother both well; had six children; eldest in perfect health; second died at 3 years of marasmus and diarrhea; third, one of the cases here reported; fourth in good health; fifth, second case here reported; sixth died at the age of 9 years.

6. Brill: Primary Splenomegaly, with a Report of Three Cases Occurring in One Family, *Am. Jour. Med. Sc.*, 1901, 1905, 1909.

CASE 1.—Male, aged 9 years, died with enlargement of the spleen.

CASE 2.—Male, aged 31 years; no malaria, rheumatism nor tuberculosis; had persistent patch of erythematous papules which extended from the malar prominence of one side across the skin covering the nasal bone to the same prominence on the other side, first observed in 1885; no splenic enlargement till 1889; occasional epistaxis. In 1899 first enlargement of liver noted; also a peculiar hard, ochre-colored, wedge-shaped infiltration of the sclerotic of the nasal side of each eye; lost weight slowly but progressively. In 1899-1900 the skin of neck, face, and hands began to be dusky (light yellow to brownish tint). In 1893 blood examination showed normal red and white count; Hgb. up to 1900 never lower than 80 per cent. In 1900 the progress of disease became rapid. The patient had an acute attack of colitis. After convalescence hemorrhagic furuncles appeared.

In 1902, pain appeared in the lower end of the left tibia; in June, 1902, the patient had a malarial attack; epistaxis became frequent. Blood, 3,200,000 reds, 8,240 whites. Hgb. 45 per cent. There was no increase in size of spleen during the attack of malaria.

In 1903 pain appeared in the ankle. Blood, 4,400,000 reds, 5,240 whites, Hgb. 55 per cent. The spleen extended 3 cm. beyond middle line and filled the iliac cavity. In 1904, ecchymoses appeared on the fibula. In March, 1904, there were dyspnea, fever and pericarditis. The patient died March 30, 1904, aged 34 years. Ascites was present for forty-eight hours before death; the glands were never enlarged. The spleen weighed 5,280 gm. Discoloration of the skin was limited to face, neck, wrists, and hands. There was no bone tenderness.

CASE 3.—Female, aged 34. Observed since 1885. In 1888 the spleen was enlarged; liver not enlarged; no glands. In 1895 the blood count was 4,800,000 reds, 7,168 whites, 80 per cent. Hgb. In 1896 the patient had typhoid fever. The color of the skin was brownish-yellow. There was frequent oozing from the gums; increasing anemia, increasing emaciation and increasing enlargement of the abdomen; infrequent attacks of epistaxis and oozing from the gums. Blood, 3,500,000 reds, 3,600 to 5,200 whites, Hgb. 35 per cent.

The patient complained of dyspnea. Sept. 12, 1904, the patient was thrown down and sustained a laceration of the brain and fracture of the skull; died same night. The spleen weighed 7,000 gm.

SCHLAGENHAUFEN'S CASE 1.<sup>1</sup>—Female, aged 41. The mother of the patient stated that the patient had enlargement of the spleen for a long time. At the age of 5 she was sent to the hospital on that account; at 21 brown pigmentation of skin of face was noted. Frequent bleeding from the gums and nose occurred. In January, 1906, the patient looked emaciated, weighed 39 kilos and a diffuse brown pigmentation of face and lower extremities was present. The spleen was enormously enlarged; liver slightly enlarged; sternum tender on pressure.

Blood: Jan. 2, 1906, 4,700,000 reds, 1,300 whites, 65 per cent. Hgb.; Feb. 6, 1906, 4,024,000 reds, 2,200 whites, 58 per cent. Hgb.; March 3, 1906, 800 whites.

May 20 the patient came in a dying condition to the hospital and died the same night. May 21, 1906, necropsy showed tuberculous glands of the neck with fistula; the spleen weighed 3,510 gm.

SCHLAGENHAUFEN'S CASE 2.—Female, aged 33, sister of the above patient, at 20 suffered from dysentery. At this time she was told by her physician that she had a large spleen. Since her tenth year her face was bronzed; had frequent nosebleeds; on cheeks and forehead broad, and under eyes, small patches of brown pigmentation; spleen enlarged to crest of ilium; liver somewhat enlarged; nodes palpable; blood, 5,735,000 reds, 3,435 whites, Hgb. 88 to 90 per cent. The patient felt fairly well and was able to work.

7. Schlagenhafen: Verhandl. d. deutsch. path. Gesellsch., 1906.

**MARCHAND'S CASE.**—Female, with a splenic tumor for twenty years; liver also enlarged; tendency to hemorrhage was noted; skin icteric; brownish color; no leukocytosis. The spleen weighed 2,720 gm.

#### ETIOLOGY

*Family Incidence:* The disease is undoubtedly congenital and usually affects more than one member in the same family. Of the cases here collected, there are three members affected in two families; two members affected in three families.

*Sex:* Many more females are affected than males. Of the sixteen cases here reported, twelve are females, four males.

*Age:* The youngest reported was 3 years, the oldest 41 years. Five of the patients were between 30 and 35 years; seven were between 3 and 10 years; one between 10 and 20 years; one between 20 and 30 years; one, age not given.

#### PATHOLOGY

In eight of the sixteen cases autopsies were performed, and in three the spleens were examined after removal by operation. In the eight autopsies performed the findings in the spleen and liver were almost identical in all the cases. Bovaird was first to note similar changes in the mesenteric glands; and Mandelbaum and Libman were the first to find the endothelial hyperplasia in the bronchial and retroperitoneal glands, and in the bone-marrow.

*Macroscopic Examination.*—The liver is firm and smooth over the greater part, and is usually much enlarged; there is evidence of old and new infarcts; on section it is chocolate colored and there are numerous small white areas.

The spleen is much enlarged; the form of a normal spleen is retained; on the external surface fibrous adhesions are present; the surface is white to yellow, and in general is smooth; the fibrous coat is thickened; the substance is firm and resistant.

The appearance of the cut section varies; a central section shows firm yellow-white areas of pyramidal form; the remainder has the appearance of normal spleen.

*Lymph-nodes* are enlarged and soft; on cross-section the central parts are deep red and the periphery is pale.

*Microscopic Examination.*—Spleen: Sections from hard white areas differ from other sections that have the appearance of normal splenic tissue. In the latter sections there are large irregular spaces filled with large, brightly stained cells. The walls of these spaces consist in part of a delicate line of connective tissue with infrequent small oval nuclei; adjoin-

ing spaces communicate with one another by narrow passages. The cells within the spaces are very large, and are of varied shape; many lie free in the spaces; these cells are round or oval. The nuclei vary considerably in size and shape; as a rule, they are very small in proportion to the size of the cell. There are also in some places giant cells. These spaces are the pulp spaces of the spleen, and the cells that fill them have sprung from their walls. The normal pulp cells have disappeared. On the other hand, the Malpighian bodies are met with almost unchanged. The connective tissue in some places is so abundant that the spaces contain but one cell.

Sections from the white areas consist of dense connective tissue. In part this is infiltrated with small round cells; in other parts seems to be made up of a meshwork of capillaries.

Capsule and trabeculæ are greatly thickened. The blood-vessels are surrounded by a greatly increased quantity of connective tissue.

The Malpighian bodies "seem very little affected by the great changes that have gone on about them."

**Liver:** The capsule is thickened and the connective tissue throughout the organ is increased; the capillaries contain considerable pigment; the liver cells are normal; the bile ducts are normal; in the blood that fills the branches of the portal vein there are large cells of the type seen in the pulp spaces of the spleen. Endothelial cells are mostly seen in the interlobular connective tissue spaces; a few are seen in the lobule proper.

**The Lymph-Nodes:** These are swollen, red and soft; each follicle is outlined by a wall of brightly shining, dark pigment. The part of the lymph-sinus not occupied by pigment is nearly completely filled with the above-described endothelial cells.

**Bone-Marrow:** Cells identical with those found in the above-described organs are also found in abundance in the bone-marrow.

#### SYMPTOMATOLOGY

1. **Enlargement of the spleen.** One of the first symptoms and signs noted by the parents and the patients is a mass in the left hypochondrium; this mass is not tender. There is a gradual but progressive enlargement of the spleen. The increase in size of the spleen in this disease is surpassed only in splenomyelogenous leukemia. It is surprising how large the spleen may become without causing any great inconvenience to the individual; and the enlargement of the spleen takes place a long time before any secondary symptoms arise. In many cases the condition is discovered accidentally, when the patients apply for treatment for other ailments. In almost all the cases the spleen passes the median line and the lower portion well fills the iliac cavity. The smallest spleen weighed 880 gm. The largest spleen weighed 7,000 gm. The average of nine

spleens was 4,000 gm. (see table). The earliest age at which the first splenic enlargement was noted was 2 years. The oldest 20. In two the splenic enlargement was noted at 3 years; in two at 4 years; in one at 5 years; in one at 7 years; in one at 15 years; in one at 19 years; in one at 20 years.

2. Enlargement of the liver. In all the cases there was a concomitant enlargement of the liver. In some cases the liver increased in size proportionally to the spleen; in others it was slightly enlarged. But in all the cases there was some enlargement of the liver. In all but one of the cases the hepatic enlargement was secondary to the splenic enlargement; and in all but one of the cases the spleen was larger than the liver. In Case 15 (see table) the liver is more enlarged than the spleen.

3. Enlargement of the lymph-nodes. The lymph-nodes are usually normal. In Cases 2 and 3 (see table) there was slight enlargement, but I think we cannot positively rule out specific infection. There is a history of a stillbirth at eight months and four deaths in early infancy in that family. I am of the opinion that the glandular enlargement was probably due to an underlying syphilitic infection. Patient 11 had tuberculous glands of the neck.

4. Blood changes. The blood shows usually a mild anemia; the anemia varies in severity from time to time, and is subject to various grades of improvement; only in later stages of the disease does it become progressive.

The lowest red blood-cell count was 2,880,000; the highest, 5,735,000; the average of seven cases, 4,100,000.

The lowest white blood-cell count was 1,300; the highest, 9,000; the average of seven cases, 5,600.

The lowest hemoglobin estimation was 45 per cent.; the highest, 88 per cent.; average of seven cases, 70 per cent.

Differential counts of six cases showed nothing abnormal.

Bone tenderness was noted in three of the sixteen cases.

5. Abdominal pain, fulness and a dragging sensation was noted in eight cases.

6. Pigmentation is described, varying from a brownish, bronzing and Roman gold color to a yellow, light-yellow, icteric hue. The pigmentation is seldom diffuse and usually affects the face, neck and extremities, the bridge of the nose, around the eyes and the cheeks being favorite spots.

7. Hemorrhages, as a rule, are not severe, but usually in the form of epistaxis or oozing from the gums; usually frequent. Patient 2 had menorrhagia. Patient 9 had hemorrhagic pericarditis, of which he died.

8. Jaundice and ascites are usually absent. Jaundice was present in two cases; ascites in Patient 9 for forty-eight hours before death.

## COURSE OF DISEASE

The course of the disease is slowly progressive, with a certain number of remissions. The shortest duration noted is three years; the longest, thirty-six years; the average duration, fifteen years. In one case the disease lasted three years; in two four years; in two, thirteen years; in two, nineteen years; in one twenty years; in one, twenty-five years; in one thirty-six years.

But few died of the disease itself; the majority usually die of inter-current diseases:

Patient 1 died of tuberculosis of the lung and peritoneum; Patient 2, after splenectomy; Patient 3, of asthenia due to the disease itself; Patient 4, of asthenia due to the disease itself; Patient 7 died three hours after splenectomy; Patient 9, of disease (pericarditis); Patient 10, of accident; fracture of skull; Patient 11, of septic cholangitis. Patient 14 died suddenly. Patients 3, 15 and 16 were still living at the time of this report.

## DIAGNOSIS

The disease which splenomegaly (Gaucher) resembles most, but from which it differs greatly, is anemia splenica. The differential points will be noted from the following:

## ANEMIA SPLENICA

Family Incidence: Not more than one in a family

Sex: Males, 39 out of 47.

Age: Low limit (9-20) High limit (58-72).

Pathology: Spleen shows a hyperplastic fibrosis, involving particularly the Malpighian bodies.

The liver shows no characteristic changes.

The lymph-glands are not enlarged and show no changes.

The bone marrow shows compensatory changes, secondary to secondary anemia.

Chronicity: Four to ten years.

Splenomegaly: Large.

Size of smallest spleen, 790 gm.

Size of largest spleen, 5,670 gm.

Average of fifteen cases, 1,883 gm.

Anemia: Secondary type.

Average red blood count, 3,425,000

Average white blood count, 3,850

Average Hgb. estimation, 47 per cent.

Hemorrhages: As a rule, hematemesis in one-half the cases; severe.

Ascites and edema: Occasionally seen.

Jaundice: Moderate in degree; veins in association with cirrhosis of the liver.

Liver: Is of normal size in most cases.

## SPLENOMEGALY (GAUCHER)

Three families with two cases; two families with three cases.

Females: 12 out of 16. 3-13; 30-41.

Spleen, liver, lymph-glands and bone-marrow show endothelial hyperplasia.

Three to thirty-six years.

Larger.

Smallest, 880 gm.

Largest, 7,000 gm.

Average of nine cases, 4,300 gm.

Simple anemia.

Average, 4,000,000 reds; 5,600 whites;

Hgb. 70 per cent.

Never hematemesis, but epistaxis and oozing from the gums.

Never.

Never.

Greatly enlarged in a majority of the cases.



**BANTT'S DISEASE**

Sex: Females 32 out of 50 cases.  
 Heredity: Not congenital; does not affect more than one member of the same family.  
 Age: Youngest of 50 patients is 12 years; oldest of 50 patients is 55 years.  
 Spleen much enlarged.  
 Liver at first of normal size; then becomes enlarged, and later diminishes in size.  
 Jaundice sometimes present.  
 Ascites usually present.  
 Blood: R. B. C., 4,330,000; W. B. C., 3,800; Hgb., 56 per cent.  
 Hemorrhages: Usually severe, in the form of hematemesis.  
 Duration seven to ten years.  
 Death: Usually due to intoxication from cirrhosis of liver or to severe hemorrhage.  
 Pathology: There is a fibrosis of the reticulum of the spleen, the liver and the portal vein. Bone marrow and lymph-glands are normal.

**SPLENOMEGALY (GAUCHER)**

Females 12 out of 16 cases.  
 Is probably congenital; usually affects more than one member of the same family.  
 Youngest recorded is 3 years; oldest recorded is 41 years.  
 Larger.  
 Always enlarged.  
 Never present.  
 Never present.  
 R. B. C., 4,200,000; W. B. C., 6,000; Hgb., 70 per cent.  
 Never severe; usually epistaxis or oozing from the gums.  
 Three to thirty-six years.  
 Usually due to intercurrent disease.  
 There is an endothelial hyperplasia of the spleen, the liver, the lymph-glands and the bone marrow.

In children it is most important to differentiate splenomegaly (Gaucher) from von Jaksch's disease (anemia pseudoleukemica, or according to more recent nomenclature, anemia splenica infantum). Differential points are as follows:

**SPLENOMEGALY (GAUCHER)**

1. Always primary.
  2. Usually affects children between the ages of 2 and 4 years.
  3. Discoloration usually yellow or orange; more marked in some parts.
  4. Spleen much larger; weighs 1,500 gm.
  5. Liver usually enlarged.
  6. Glands (lymph) never enlarged.
  7. Blood: Red blood corpuscles, 4,100,000; white blood corpuscles, 5,800; Hgb., 70 per cent.
- No abnormal cells found.

**VON JAKSCH'S DISEASE**

1. Usually secondary to gastro-intestinal disease, malnutrition, tuberculosis, lues, etc.
  2. Affects children between 6 months and 2 years.
  3. No discoloration, but there is extreme pallor of whole face, which may be olive color.
  4. Spleen enlarged but not to the same extent seen in S. (Gaucher). Spleen weighs 350 gm.
  5. Liver usually not enlarged.
  6. Lymph-glands sometimes enlarged.
  7. Blood: Red blood corpuscles, 2,500,000 to 3,000,000; white blood corpuscles, 10,000 to 20,000; Hgb., 45 per cent.
- Myelocytes and normoblasts in 25 per cent of the cases.

Some of the other conditions from which splenomegaly (Gaucher) should be differentiated are: pernicious anemia, polycythemia, leukemia, aleukemic leukemia, cirrhosis post leukemia, status thymicus, cirrhosis post myxedema, abscess of spleen, lues, tuberculosis, malaria, etc., and the cirrhosis due to different causes, as alcoholic, hematogenous, cardiac,

metabolic, chromatic, adenomatosa, and that due to tuberculosis, distoma and the infections.

#### SUMMARY

1. Splenomegaly (Gaucher) is a distinct disease.
2. It is probably a congenital condition, and usually affects more than one member of the same family. Females are more susceptible to this disease than are males (3 to 1).
3. The first symptoms may appear as early as the third year or as late as the twentieth year.
4. The spleen becomes enormously enlarged and is followed by an enlargement of the liver (but the enlargement of the liver is not as great as occurs in the spleen).
5. Vague abdominal pains are present. There is pigmentation of the face and hands, the color being brown, yellow or bronze.
6. Hemorrhages, if present, are not severe; usually are in the form of epistaxis or oozing from the gums.
7. The disease is slowly progressive and is marked by periods of temporary improvement. The disease may last from three to thirty-six years.
8. The majority usually die of intercurrent diseases; but few die of the disease itself.
9. At autopsy there is found an endothelial hyperplasia in the spleen, liver, lymph-nodes and bone-marrow.

In conclusion I wish to express my indebtedness to Dr. Herrman, by whose courtesy I am enabled to report the cases of the clinic. I also wish to express my thanks to Dr. E. Cleaver, who performed the blood examinations on the patients here reported.

1967 Seventh Avenue.

## THE TREATMENT OF PERTUSSIS WITH VACCINE \*

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The seriousness of pertussis in the infant, its tendency to be complicated by pneumonia, emphysema, convulsions and perhaps paralysis, and the possibility of a fatal termination, have caused this disease to occupy a prominent place in the minds of all physicians, particularly as it is so commonly seen in infancy, 50 per cent. of all cases occurring in the first two years of life. As the treatment of pertussis by drugs is so unsatisfactory, it is important that any new treatment that offers a reasonable hope of success should be thoroughly tested.

Pertussis is undoubtedly contagious and positively due to a micro-organism, and it seems to me that the bacillus described by Bordet and Gay in "Studies in Immunity" has many claims to the position of the specific pathogenic organism.

Bordet and Gengou<sup>1</sup> claim to have found the true bacillus of pertussis. They assert that the bacillus is found only in the early period of the disease, and only that part of the expectoration which comes from the region in which the bacteria are most active should be used; i. e., "the products from the depths of the bronchi, expectorated during the periodic accesses of the disease." This exudate contains the true bacillus in considerable numbers and, in favorable cases, in almost pure culture. "As the disease progresses, on successive days fewer and fewer specific bacilli are found and phagocytosis is more frequent than earlier." They emphasize the importance of studying cases not complicated with other respiratory affections, and of avoiding the study of the sputum of hospital patients, as in the latter other organisms are apt to be present in great numbers.

They describe the micro-organism of pertussis as "little ovoid bacilli, somewhat elongated at times, but frequently so short as to resemble a micrococcus." With Kuhne's carbolated blue stain, the bacilli will stain a pale blue, and the outline of the bacillus, and particularly its poles, are frequently more deeply stained than the center. "This organism was found scattered indiscriminately among the cells and was at times within cells." It was negative to Gram's stain.

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\*Read before American Pediatric Society, Lake Mohonk, June 2, 1911.

1. Bordet and Gengou: *Studies in Immunity*, 1906, chap. xxvii.

This bacillus does not grow well on blood-agar. It develops well in a liquid medium of 1 per cent. glycerinated bouillon with equal parts of rabbit's blood or serum. It is found that the organism grows only under the best condition of aerobiosis.

"The authenticity of this bacillus as the causal agent in whooping-cough rests in large part on the circumstances in which it is found, namely, the excessive growth of the organism in pure culture during the initial period of the disease in young children who have never been ill. The principal argument, however, in favor of this organism appears to be furnished by a study of the specific properties of the serum. The serum of individuals who have never had whooping-cough, or who have had it a long time before, does not agglutinate the bacillus even in low dilution. The serum of children who have recently recovered from the disease has a moderate agglutinating property which is constant and evident. The most remarkable fact, however, is the intensity of the sensitizing property in such serums."

Bordet and Gengou assert that the organism described by Pfeiffer resembling the influenza bacillus, "acts no differently with whooping-cough serum than it does with normal serum." They find that the serum of children suffering from, or convalescent from whooping-cough, shows very inconstant agglutinating properties. An agglutinating property in a mild form is frequently present; it may be entirely lacking. They find, however, that the alexin fixation method always gives marked positive results.

Bordet, as described in a later communication (1908), has obtained from the organism an endotoxin. He and his co-worker hope to obtain an antitoxic serum by injecting endotoxin instead of bacteria, and claim that the bacillus produces a poison that causes a necrosis of that portion of the epithelium covering the bronchi where rapid increase in the number of the bacilli occur, and that this necrosis is the cause of the characteristic symptoms of pertussis and their persistence.

As I was without any previous knowledge of the amount of vaccine to administer and was consequently ignorant as to the number of bacteria to inject, my earliest patients received only 20 million bacteria every four days. This dose failed to produce any untoward symptoms locally or constitutionally, and was increased to 40 million bacteria every four days. A careful study of the patients receiving this dose, by all those coming in contact with the patients, including parents, other physicians and myself, tended to show that the disease was apparently being modified by the treatment. The same dose was then given every three days, and the beneficial results seemed to be distinct. The number of paroxysms of coughing became less; the severity of the paroxysms diminished, cyanosis was less marked, vomiting during the coughing was less frequent, and the children, as a rule, slept better and were less disturbed at night, since the number of characteristic attacks became less. The dose of 40 million was retained, but the injection was now given every two days. The num-

per of injections given varied from six to eight. No case has been recorded in which less than six doses were administered, and none of the patients received more than eight injections of 40 million each, except twenty-two, who had nine injections. In not a single instance were evidences of local inflammation noticed at the site of the injections, and while most of the injections were given in the loose tissues of the scapular region, some children received injections into the arms.

The interscapular region is, in my judgment, the best place for injection, as it is difficult for the child to scratch this portion of the body, and it is apt to be fairly well protected by clothing. Care was taken to render the part injected clean with soap and water and alcohol and to sterilize the hypodermic syringe. Neither I nor any other physician to whom I gave the vaccine noticed any local or constitutional effects from the remedy; rashes, joint pains and fever were carefully looked for, but were never observed.

All but one of the cases were in private practice, and this affords a much better test of the efficacy of the remedy than a study of hospital cases. Institution children in whom whooping-cough develops while in the ward, are immediately sent to the pertussis pavilion, and are apt, therefore, to be in intimate contact with other pertussis patients, who may have other infections of the respiratory organs. Moreover, institution children do not, as a rule, do well when attacked by infections, and are therefore less apt to show the true beneficial effects of which a remedy is capable. I do not wish to be understood as suggesting that it should not be used on hospital patients, but they are manifestly less apt to exhibit the true influence of the remedy, as they are, as a class, less vigorous and robust than children living outside of institutions. This, of course, applies more to children under 2 years of age. Older children are less apt to be affected with hospitalism. Outside children admitted to hospitals with pertussis are apt to be received late in the disease and commonly have some complication, often pneumonia. I would strongly advise that all these children be given the benefit of the vaccine treatment; I believe that a thorough trial of it in these cases will demonstrate its efficacy; but for the purpose of this investigation and study, private cases are better.

Physicians are apt to be too optimistic in ascribing to new drugs or methods of treatment curative properties. A more extended trial may prove their conclusions to be premature and unfounded, and this may be the fate of pertussis vaccine. In order at least partially to eliminate this error, those coming in intimate, daily contact with the patients, parents, nurses and other members of the household, have been systematically questioned, and their opinions, in the large majority of cases, have been in favor of the remedy—that it tends to diminish the severity and number of the attacks and shorten the course of the disease.

After the injections were stopped, the cases were followed as closely as possible to see whether the usual course of the disease was influenced only during the use of the remedy, and whether the paroxysms of coughing would return after the discontinuance of the vaccine. This method of following the cases resulted in showing that improvement almost invariably continues steadily after the course of treatment by the vaccine has been discontinued.

It is, of course, well known that epidemics of pertussis differ greatly in their severity, and it may be that future cases will be less influenced by the treatment than those cases on which this paper is based. I have seen personally many of these cases, and in my judgment they were cases of ordinary severity. In the list of cases here reported, no child was included who did not have the typical whoop, and this typical whoop was heard by the attending physician in each instance. The judgment of the parents or nurse was never taken on this point.

In all, twenty-four cases of pertussis are reported. The ages of the children were as follows:

	Cases
Less than 6 months .....	3
6 months to 1 year .....	2
1 to 2 years .....	4
2 to 4 years .....	10
4 to 8 years .....	5

#### REPORT OF CASES

CASE 1.—Mary H., aged 3 years, colored, pertussis ward, Philadelphia Hospital; first injection given March 14, 1911; whooping two weeks before treatment began; received six injections, three of twenty million, three of forty million. A careful systematic daily record was kept of the number of the paroxysms in every twenty-four hours, of the duration in minutes and seconds of each paroxysm, whether severe, moderate or mild, and the frequency of vomiting produced by the paroxysms of coughing. Careful records of the temperature, pulse and respiration were recorded only in those cases in which there was fever. The record shows that the child was much benefited by the treatment. The paroxysms were reduced from an average of twenty in twenty-four hours to five in twenty-four hours. The duration of the paroxysms was much shortened. They were less in severity, and the frequency of the vomiting attacks diminished. The temperature, respiration and pulse all improved. From March 14 to 20 the temperature varied from 101.5 to 100 F.; March 21 to 24, from 101 to 100 F.; March 24 to 28, 101 to 100 F.; March 28 to April 1, 100 to 99 F.; April 1 to April 8, normal.

There is no doubt in my mind that the child was distinctly benefited by the treatment. The records kept in the hospital are too voluminous to publish. However, the portion of the record here appended is of interest.

#### HOSPITAL RECORD OF MARY H.

Admitted to whooping cough isolation ward March 1, 1911. Received vaccine lymph (pertussin), 20,000,000, March 14, 1911.

First dose March 14: March 14, 4 p. m., to March 15, 4 p. m., total number of times coughed, 18; coughed hard 14 times; vomited, 7 times; coughed not so hard, 4 times; expectorated, 7 times.

March 15, 4 p. m., to March 16, 4 p. m., total number of times coughed, 12; coughed hard 5 times and vomited; coughed hard 7 times and expectorated.

March 16, 4 p. m., to March 17, 4 p. m., total number of times coughed, 11; coughed not so hard, 4 times; coughed hard, 4 times; coughed hard and vomited, 3 times.

Second dose, March 17: March 17, 4 p. m., to March 18, 4 p. m., total number of times coughed, 10; coughed not so hard, 4 times; coughed hard, 3 times; coughed hard and vomited, 3 times.

March 18, 4 p. m., to March 19, 4 p. m., total number of times coughed, 13; coughed hard and vomited, 6 times; coughed hard, 7 times.

March 19, 4 p. m., to March 20, 4 p. m., total number of times coughed, 11; coughed hard and vomited, 5 times; coughed hard, 6 times.

Third dose March 20: March 20, 4 p. m., to March 21, 4 p. m., total number of times coughed, 8; coughed not hard, 4 times; expectorated; coughed hard, 4 times, vomited.

March 21, 4 p. m., to March 22, 4 p. m., total number of times coughed, 8; coughed not hard, 4 times; expectorated; coughed hard, 4 times; vomited.

March 22, 4 p. m., to March 23, 4 p. m., total number of times coughed, 9; coughed not so hard, 4 times; coughed hard, 5 times; vomited, 4 times.

Fourth Dose, March 23: March 23, 4 p. m., to March 24, 4 p. m., total number of times coughed, 8; coughed not hard, 3 times; coughed hard, 5 times; vomited 3 times.

March 24, 4 p. m., to March 25, 4 p. m., total number of times coughed, 6; coughed not hard, 2 times; coughed hard, 4 times; vomited 3 times.

March 25, 4 p. m., to March 26, 4 p. m., total number of times coughed, 6; coughed not hard, 1 time; coughed hard, 5 times; vomited 3 times.

Fifth Dose, March 26: March 26, 4 p. m., to March 27, 4 p. m., total number of times coughed, 6; coughed not hard, 3 times; expectorated; coughed hard, 3 times, vomited.

March 27, 4 p. m., to March 28, 4 p. m., total number of times coughed, 6; coughed not so hard, 3 times; coughed hard, 3 times; vomited 2 times.

March 28, 4 p. m., to March 29, 4 p. m., total number of times coughed, 5; coughed not so hard, 1 time; coughed hard, 4 times; expectorated 4 times; vomited 1 time.

Sixth Dose, March 29: March 29, 4 p. m., to March 30, 4 p. m., total number of times coughed, 5; coughed not hard, 2 times; coughed hard, 3 times; vomited 2 times; expectorated 3 times.

March 30, 4 p. m., to March 31, 4 p. m., total number of times coughed, 5; coughed not hard, 1 time; coughed hard, 4 times; expectorated 3 times; vomited 2 times.

March 31, 4 p. m., to April 1, 4 p. m., total number of times coughed, 8; coughed not hard, 3 times; coughed hard, 5 times; vomited 3 times.

April 1, 4 p. m., to April 2, 4 p. m., total number of times coughed, 6; coughed not hard, 1 time; coughed hard, 5 times; vomited 3 times.

CASE 2.—Elizabeth H., aged 3 years and 10 months; report by Dr. E. D. Grier; treatment began April 11, 1911. The child had been coughing and whooping several weeks before the first dose of pertussis vaccine was given. She received five injections of twenty million and three of forty million each. The attack was of moderate severity. The child was much improved at the end of the treatment. The cough was almost gone and there was very little whoop.

The following is a brief résumé of the notes kept by the mother, a very intelligent woman.

April 11, 1911.—From 6 to 12:15 a. m. had coughed ten times; vaccine given at 12:15; coughed five times from 12:15 until 8 p. m.; vomited twice slightly.

April 12, 1911.—Coughed once during the night; coughed four times from 6 a. m. until 12 M.; vomited once; coughed three times from 12 M. until 6 p. m.; in all eight paroxysms.

April 13, 1911.—Coughed twice during the night; coughed four times during the morning, and four times during the afternoon; no vomiting.

April 14, 1911.—Coughed once during the night; no vomiting; coughed seven times during the day; appetite good.

April 15, 1911.—Coughed once during the night, about 5 o'clock; coughed seven times during the day; vomited once after taking 10 ounces of milk. Dr. Grier administered vaccine at 10 a. m.

April 16, 1911.—Coughed once during the night about 5 o'clock, but not since 4:30 the previous evening; seven times during day. Vomited once slightly.

April 17, 1911.—Coughed six times; vomited most of the first bottle of milk at 6:30 a. m., but ate a good breakfast. She takes a nap every morning of 1½ hours; seems much improved. The worst coughing spell is in the morning when she has some trouble in bringing up the phlegm.

April 18, 1911.—Coughed early in the morning; seven times during the day, and vomited a very small amount in the afternoon. "Severe cough at 3:30 p. m., while I was present."—Grier.

The baby received the last dose of vaccine May 6, and under this date Dr. Grier writes me as follows: "The family feel that the child is much improved, and the attack I heard to-day bears out their statement, as it was of no moment; the cough now is almost nothing."

CASES 3 AND 4.—Edwin W. and Kenneth W., brothers, aged 7 years and 4 years; first injection of pertussis vaccine April 11, 1911. Each received eight injections of forty million. Both had been whooping about one week before the treatment began. Both were benefited by treatment, the older boy more than the younger. In both children the number and severity of the paroxysms diminished. The younger boy had adenoids and tonsils removed May 20, six weeks after the beginning of the vaccine treatment. He was so much better that we did not hesitate to place him in a private room in a hospital for the removal of his adenoids and tonsils.

CASE 5.—William N., aged 15 months; first injection of pertussis vaccine May 10, 1911; whooping five days before treatment began; received eight injections of forty million each. After the sixth injection the child had a slight bronchopneumonia; temperature varied from 101 to 103 F. for five days. The vaccine treatment apparently did not affect the pertussis in any degree whatever. The patient in my opinion was not benefited by the treatment. At the end of the treatment the boy was still coughing and whooping, but neither the cough nor the whoop was severe in character and the boy's temperature was normal. I believe that the dose in this case was insufficient to produce an effect. Instead of forty million, he should have been given at each dose eighty to 100 million.

CASE 6.—Francis N., 2½ years old, sister of Patient 5; first injection of pertussis vaccine May 10, 1911; whooping two weeks when treatment began. A severe case; numerous paroxysms day and night; vomited frequently, and often during attack became cyanosed; eight injections of forty million each were given. The paroxysms of coughing after the child had received four injections were distinctly less severe, although not diminished in number. After receiving the full number of injections, eight, the boy was much improved. The paroxysms were few in number, and very light, with only an occasional whoop.

CASE 7.—Isabella L., aged 4 months; whooping two weeks before treatment began; eight injections of forty million each were given; much improved; very little cough and occasional whoop. This child had a mild attack of pertussis, and at the end of treatment was practically well. Very little cough remained and hardly enough whoop to designate it by that name.

CASE 8.—David L., aged 2 years; first injection of pertussis vaccine May 12, 1911; whooping one week before treatment began; seven injections of forty million each were given. A careful record of the number and severity of the attacks was made. In the early part of the treatment the attacks were very severe; thirty-six in twenty-four hours. At the end of the treatment the attacks averaged



about twenty-eight in twenty-four hours. There was no decrease in the severity of the attacks. The patient was apparently not benefited by the treatment. The case was reported by Dr. W. S. Lucas. I believe the dose of vaccine used in this case was too small. In a similar case I would advise eighty million or 100 million with each injection.

CASE 9.—Charles L., aged 8 years, brother of Patient 8; first injection of pertussis vaccine May 10, 1911; whooping ten days before treatment began. This was a much milder case than that of his brother, David L., Case 8. Patient 9 received eight injections of forty million each. At the beginning of treatment, he averaged fifteen paroxysms in twenty-four hours, moderately severe in type, about five or six attacks occurring at night. At the end of treatment he averaged about six or seven attacks in twenty-four hours, very mild in character, and not more than one or two at night. The boy was evidently much improved by treatment. Reported by Dr. W. S. Lucas.

CASE 10.—Fanny C., colored, aged 5 months; first injection of pertussis vaccine given May 5, 1911; a sturdy child, breast-fed, always in good health until the attack of pertussis. Paroxysms occurred every hour during the day and three or four times at night, vomiting with almost every paroxysm; face became deeply congested with each attack of coughing. Six injections of forty million each were given; there was so much improvement at the end of the sixth injection that the mother considered the child well and wished the treatment discontinued. The child still coughed and whooped occasionally, but the paroxysms were very mild.

CASE 11.—Male, aged 5½ years; reported by Dr. S. M. Wilson; whooping one week before treatment began; eight injections—three of twenty million, four of forty million and one of sixty million; first injection April 29, 1911. Dr. Wilson wrote me as follows: "At the time of his first injection, he had twenty or more severe paroxysms daily and his sleep at night was badly disturbed by them. At the end of the treatment he rarely coughs, and when he does, there is usually only a single effort and no expectoration." Dr. Wilson considered that the boy was very much benefited by the treatment.

CASE 12.—Cecil D., aged 3 years; first injection of pertussis vaccine May 5, 1911; reported by Dr. H. W. Gregory. The child had been whooping three weeks before treatment began. The attacks were severe, occasionally producing hemoptysis; eight injections of forty million each were given. At the end of the treatment the child was practically well, averaging only one mild paroxysm during the night and with very little cough during the day.

Cases 13, 14, 15, 16 and 17 all occurred in the practice of Dr. S. M. Cleveland, and according to Dr. Cleveland's observations the patients were apparently not benefited by the treatment. The only explanation that I am able to give for the failure of the treatment in these cases is that the dose of vaccine used was not large enough. A brief history of these cases follows:

CASE 13.—Carl O., 16 months old, whooping five days when treatment began; seven injections of forty million each produced apparently no benefit.

CASE 14.—Dorothy O., sister of Patient 13, aged 4 months; whooping seven days; given seven injections forty million each; apparently no benefit from treatment.

CASE 15.—Elizabeth O. B., 10 months old, sister of Patient 16; coughing two months before treatment began; six injections of forty million each were given; apparently no benefit resulted from treatment.

CASE 16.—Marie O. B., aged 5 years; coughing for two months before treatment began; six injections of forty million each were given, with no benefit.

CASE 17.—James O. B., aged 7 years, brother to Patients 15 and 16; coughing two months before treatment began; six injections of forty million each were given, with no benefit.

CASE 18.—James L., aged 28 months; first injection of pertussis vaccine given May 9, 1911; whooping three weeks when treatment began; eight injections of forty million each were given. The patient was a delicate boy and was having paroxysms hourly day and night, with occasional vomiting. The patient began to improve after the first injection; vomiting ceased after the second injection. At the end of the treatment there was a little cough, but no whoop. Reported by Dr. John A. McCormick.

CASE 19.—John L., aged 2 months, brother of Patient 18, was given the first injection of pertussis vaccine May 9, 1911; whooping three weeks before treatment began; eight injections of forty million each were given. The case was moderate in severity, and the patient was apparently much benefited by treatment. At the end of the treatment the cough occurred less frequently; the paroxysms were mild. Reported by Dr. John A. McCormick.

CASE 20.—Genevieve B., aged 15 months; treatment began May 8, 1911, after whooping had existed four weeks. The first injection of pertussis vaccine was on May 8; eight injections of forty million each were given. At the beginning of treatment the child had about sixteen paroxysms in twenty-four hours, ten during the day and six during the night. The paroxysms were very severe, with frequent vomiting and cyanosis; improvement began after the third injection; distinct improvement was noticed after the fifth injection. At the end of treatment the child was still coughing, but only an occasional whoop. Reported by Dr. John A. McCormick.

CASE 21.—John B., aged 3 years, brother of Patient 20; first injection of pertussis vaccine May 8, 1911; whooping three weeks when treatment began; eight injections of forty million each were given. The case was of more than ordinary severity. The paroxysms occurred about once an hour day and night, with cyanosis and vomiting. The cyanosis and vomiting disappeared after the fourth injection. After the fifth injection, the mother thought the child was well enough to stop the treatment; eight injections, however, were given. At the end of the treatment, the child was almost entirely well, with practically no cough and no whoop. Reported by Dr. John A. McCormick.

CASE 22.—Edward S., aged three years, treatment began May 8, 1911. Hemorrhage into the conjunctiva occurred as the result of the severity of the paroxysms. No improvement was noticed until after the fourth injection. Vomiting ceased after the sixth injection. The patient received nine injections of forty million each. At the end of the treatment the boy was very much improved, although he still coughed and whooped occasionally. Reported by Dr. John A. McCormick.

CASE 23.—Emma M., aged 9 months; first injection of pertussis vaccine May 6, 1911. Whooping commenced one week before treatment began. Seven injections of forty million each were given. Cyanosis and vomiting were frequent at the beginning of treatment. Paroxysms occurred at least every hour during the day and five or six times during the night. At the end of the treatment the paroxysms were few in number and less severe, but the child was still coughing and whooping occasionally. Reported by Dr. Scott Lau.

CASE 24.—William B., aged 5 years; first injection of pertussis vaccine May 8, 1911; whooping eleven days before treatment began; eight injections of forty million each were given. The case was one of moderate severity. At the end of treatment the paroxysms of coughing were much fewer in number and less severe, although the boy still coughed and whooped occasionally. He was distinctly benefited by the treatment. Reported by Dr. Scott Lau.

These reports do not represent the true worth of the remedy, as I believe better results would surely have been obtained had larger doses of the vaccine been employed; 40 million may be, and probably is, a sufficient dose for a mild case in an infant or young child. One hundred million

would be a much more suitable dose for a severe case, regardless of the age of the patient.

Of the twenty-four reported cases, seven were apparently not benefited by the treatment, the disease evidently pursuing its usual course in about 29 per cent. Seventeen patients, or about 71 per cent., were apparently benefited by the treatment. I believe the dose could, and should, be increased beyond 40 million, especially for severe cases; 60, 80 or 100 million will probably be a more efficient dose. The results obtained in these twenty-four cases warrants, in my opinion, a more extensive trial of the vaccine.

## RESUSCITATION OF ASPHYXIATED INFANTS BY THE INSUFFLATION METHOD OF MELTZER AND AUER

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The remarkable experiments of Meltzer and Auer on intratracheal insufflation were made known in France by Carrel, who also brought them to my attention. I was greatly impressed by them and concluded that the principle might be applicable to the resuscitation of asphyxiated infants, for which purpose I had an apparatus constructed by Mr. Lépine of Lyons. The apparatus is very simple and resembles the one used on animals at the Rockefeller Institute and differs only in being of a size suitable to new-born infants.

I have employed this apparatus and the method of intratracheal insufflation in my obstetrical service since August, 1910, with promising and highly interesting results. I make this statement because I am of the opinion that it will require several years' experience to determine its exact clinical value and extent of applicability. I am, however, ready to affirm that the principle of the method embodies a great advance and its efficiency is already beyond question for the reanimation of asphyxiated infants.

The principle of the method of Meltzer and Auer is well known. A continuous current of air directed as far as the bifurcation of the trachea through a tube of small caliber, produces a ventilation of the lungs sufficient for oxygenation of the blood even if there are no respiratory movements. The air injected into the bronchi returns between the catheter and the tracheal wall, and can also remove foreign bodies and mucus that may be in the respiratory tubes. The apparatus constructed by Lépine is composed of:

1. A rubber bulb.
2. A T tube, one branch of which is united to the bulb, and another to a small mercury manometer, while the third is connected to a rubber tube ending in a metal cone.
3. A gum catheter No. 12. A rod of soft copper is placed in the catheter in order to give it the proper shape for introduction into the glottis. The caliber of the catheter was selected after an anatomic study of the trachea on the cadaver. The internal diameter of the trachea of a new-born child is 4 mm. There is allowed, therefore, between the wall of the trachea and a catheter No. 12 (Charrière) a sufficient space for the

returning current of air. The end of the catheter must reach the bifurcation of the trachea. This point is located at a distance from the mouth which varies according to the size of the child. For a child weighing 2,000 gm. the distance is 8 cm.; 3,000 gm., 10 cm.; 4,000 gm., 12 cm. Therefore, three transverse lines are marked on the catheter to indicate how far it should be introduced according to the weight of the child.

#### OPERATIVE PROCEDURE

The mucus contained in the throat of the infant in a condition of asphyxia is rapidly removed by the finger or by a little sponge fixed in forceps. The infant is wrapped in a warm blanket and placed on a table, the neck being in slight hyperextension.

The index finger of the left hand of the operator is introduced as far as the upper end of the esophagus so as to feel the hard rounded prominence which is formed by the posterior face of the larynx, the two arytenoid cartilages, and to find in front of them a soft opening, which is the glottis. The catheter, containing its copper rod, to which a proper curve has been given, is introduced by the right hand between the tongue of the child and the palmar face of the left index finger of the operator and thus penetrates easily into the trachea.

The catheterization is exceedingly easy. After a few trials on the cadaver, I could always do it without trouble. Moreover, the interns, externs, and nurses of my service succeeded also in introducing the catheter very easily. The average nurse can certainly acquire the technic without difficulty.

When the catheter has reached the proper distance, the copper rod is removed. The end of the insufflation apparatus is now attached to the catheter and air is injected through the catheter by the rubber bulb, while the mercury manometer is watched. The pressure must not exceed 10 or 15 mm. Soon the noise of the returning current of air passing through the lips of the child is heard. The manometer indicates that there is no over-pressure by accumulation of air in the respiratory apparatus. Therefore, the conditions of ventilation are known, and no accident is to be feared.

The insufflation is continued as long as is necessary. After a few minutes, the child appears to be less atonic, the heart becomes stronger and more regular, and the respiratory movements start. The catheter is removed when the infant is in a condition to carry on automatic respiratory movements.

#### CLINICAL RESULTS

The method must be applied under well-defined conditions. If it is used in mild cases of asphyxiation, it is certain that it will give constant positive results as do all the other methods. If it is used in the cases in

which apparent death is not due to asphyxiation but to traumatism of the brain or of the medulla oblongata, it will yield negative results. Therefore, the value of the method must be ascertained in the cases of deep asphyxia of the new-born by long intra-uterine compression or by interference with the fetal-maternal circulation, as, for instance, from compression of the umbilical cord.

I have employed the method in seven cases of the last kind. The seven infants were restored to life after a longer or shorter period of insufflation, although two of them had been extricated after difficult versions.

*Observation 1.*—Child weighing 2,760 gm.; Braxton Hicks version for placenta prævia; no respiratory movements; heart regular, but very slow; insufflation for twelve minutes; afterward, movements of the face and respiratory movements. The child cried as the catheter was removed.

*Observation 2.*—Child weighing 4,200 gm.; difficult version, with prolonged extraction of the head; asphyxia pallida; irregular heart; a few diaphragmatic convulsions; very infrequent. Reanimation occurred after insufflation during eight minutes.

*Observation 3.*—Child weighing 3,600 gm.; extracted by forceps; probable prolapsus of cord; child was atonic, without respiratory movements; meconium evacuated; heart hardly perceptible. Reanimation occurred after insufflation during seven minutes.

*Observation 4.*—Child in a condition of blue asphyxia, but the heart was almost normal. The child was quickly reanimated.

*Observation 5.*—Similar to Case 4. It is probable that in these two cases the reanimation would also have taken place easily if the ordinary methods had been employed.

*Observation 6.*—Child weighing 1,970 gm.; premature labor; high forceps delivery; asphyxia pallida; no respiratory movements; very irregular and slow heart; grave form of apparent death. After five minutes of insufflation the heart became regular; reanimation after eight minutes.

*Observation 7.*—Child weighing 3,000 gm.; long labor; period of expulsion lasted five hours; blue asphyxia. Reanimation occurred after insufflation for six minutes.

The method deserves to be employed also in cases of traumatism to the skull and brain. I am of the opinion that it will excel other methods in this condition, although it will, of course, be limited by the severity of the injury, which may be incompatible with life.

# PROGRESS IN PEDIATRICS

## ANATOMY, PHYSIOLOGY AND HYGIENE

### Milk-Station Work and the Reduction of Infant Mortality

(*Godfrey R. Pisek: New York Med. Jour., Nov. 25, 1911, p. 1065*)

During 1911, New York City conducted a campaign against infant mortality through milk stations sufficiently comprehensive to show definite results. New York has 125,000 births yearly. Various private philanthropies have been dispensing modified milk to indigent mothers for some years. In 1911, the Committee for the Reduction of Infant Mortality established thirty-one milk depots and in addition secured an appropriation for the establishment of fifteen stations under the control of the health department, making seventy-nine stations in all. To secure cooperation of all the different agencies, the Association of Infants' Milk Stations was formed in June, 1911, and 74,000 quarts of milk were distributed weekly. The work was not confined to the distribution of milk, however, Education of the mothers was the most important factor. The intimate contact of the visiting nurse with the mothers in their homes made it possible to teach the modification of milk according to the doctor's instructions. In this work whole milk was used for the most part, modified in many instances with gruels and ordinary granulated sugar, which was found satisfactory. Deterioration in the homes was prevented by the use of inexpensive home-made refrigerators. Mothers were encouraged to continue breast-feeding where this was possible. Special diet lists were prepared for older children. Another feature of the work was the assistance and advice given in regard to protecting from infectious diseases and ophthalmia. The Association issued weekly bulletins giving comparative statistics of infant mortality in different cities. Three hundred and fifty-five cities cooperated in this. The results of the work in New York in figures were as follows: The number of deaths of infants from all causes under one year of age during the first nine months of 1911, was 11,733; while during a corresponding period of 1910 the deaths reached 12,920; in other words, there was a comparative death-rate of 124.6 in 1911, against 142.3 in 1910, a decrease of 17.7 per thousand among infants. This rate continued throughout the remainder of the year would result in a saving of 1,640 babies during the year.

Even more striking than the statement that 1,187 fewer deaths occurred up to October 1 compared to 1910, is the fact that during the months of July, August and September there were 1,244 fewer deaths than the previous year. To show that this comparison is not made with an excessively high year, it might be mentioned that there had been a decrease of 1,417 deaths from the average for these months during the five years 1906 to 1910.

In the Borough of Manhattan, from January to June, there was an increase of deaths from diarrheal diseases of 28 per cent. over the previous year, but during the month of June, after beginning the milk campaign, there was a decrease of 50 per cent. over the previous year. In July, which was exceedingly hot, there was a decrease of 60 per cent., August 23 per cent., September 25 per cent., the average decrease being 41 per cent. Comparing these results with those in other cities reported on, it was found that the diminished mortality was in direct relation to the effective preventive measures employed. Comparison between districts in the congested quarters, with and without milk stations, showed a gain over the previous year of 29 per cent. in the milk-station districts as against an increase of 9 per cent. in those without milk stations. It is felt that the best feature of the work is the educational feature.

**Suggestions for the Reduction of Infant Mortality**

(*S. Josephine Baker: New York Med. Jour., Nov. 25, 1911, p. 1067*)

The infant mortality rate is the index of the sanitary progress of any community. No one line of endeavor, however vigorously worked out, will permanently lower the death-rate, and Baker believes there is serious danger in assuming that total reduction in death-rate in any one year is wholly due to the specific efforts made during that year. The keeping of babies well cannot be worked out with the accuracy of a scientific theorem, but the fundamental principle is that prevention of diseases must be the aim and education the main weapon. Specifically, the principles of the reduction of infant mortality include:

1. The study of the problem of the institution baby. During 1911 up to October 1, 42 per cent. of all deaths of babies under one year in the Borough of Manhattan occurred in institutions, the foundling babies furnishing the greater proportion.
2. A supply of milk for infant feeding at a price within the reach of the majority of people. The relative value of raw and pasteurized milk for infant feeding still seems an open question. Purification cannot take the place of purity, but the matter is economic, and purity seems beyond our reach at the price we can pay.
3. The broadening of courses in pediatrics in our medical colleges, so that they may assume the importance that is their due and assure to every physician a thorough knowledge of infant hygiene and care.
4. The interest and attention of social students and workers, and of philanthropists, in meeting individual family needs and adjusting economic conditions.
5. Instruction of each mother, first in the necessity of nursing her baby, and, if that is impossible, then in the proper substitute feeding, and how she may take advantage of and apply the essential methods of hygienic baby care.
6. A right understanding of the immediate causes of infant mortality.

Baker then enters into the statistics of 1911 as given in an abstract of a paper by Pisek in this issue. The figures show what may be accomplished by the application of the principles enumerated above but Baker believes a more comprehensive program is necessary. Such a program would be as follows:

1. A comprehensive and wide-spread campaign of educational publicity—one that will reach both the public and the individual mothers.
2. A study of the decrease that has already taken place in the infant death-rate shows that this decrease has occurred in the three groups of contagious, diarrheal and respiratory diseases, in the order given. The group classed as congenital debility shows practically no decline. Here we need the help of the obstetrician, who should not limit the control of his patient to the confinement and the few succeeding weeks, but should insist that the mother place herself under his care and follow his directions during the entire period of pregnancy.

In order to meet and overcome this abnormal death-rate from congenital causes, we must have:

- A. Proper education and control of midwives, who in New York city care for over 40 per cent. of the births.
- B. Classes for and supervision of pregnant women, using all means to provide them with essential instruction and the means of applying it.
- C. A form of insurance that will provide a stated payment for women for a period of at least one month before and one month after confinement, thus obviating the necessity for physical labor on their part during this time.
- D. The cooperation of philanthropic forces, relief agencies, and social workers, to provide proper food, hygienic surroundings and freedom from anxiety for the mother during the prenatal period of the child's life.



The socialist will say that the crux of this whole matter is the living wage for the wage earner of the family. To a great extent Baker agrees with him. Such a solution would lighten our labors but we should still have to consider the vast and vexed question of the illegitimate child.

3. The question of institution care versus the placing out system for foundling babies is one that should be practically worked out. The death-rate in these institutions is abnormally high. This rate is greatly reduced when the babies are boarded out and receive that individual attention which every baby needs. Foundling institutions should serve as clearing houses only, furnishing hospital care for the sick babies and immediately placing all others out in properly supervised private homes.

4. Next it is essential that we realize that infant mortality is a year round problem. Misled by the usual increase in summer, we have confined our efforts mainly to that time of the year. The time to save the baby is before it gets sick—not afterward.

#### **Infant Mortality and Morbidity in Berlin in the Summer of 1911**

(*Ludwig F. Meyer, Deutsch. med. Wchnschr., Nov. 9, 1911, p. 2090*)

For a solution of the summer mortality of infants Prausnitz has investigated the figures so far obtained. Meyer regards it as especially necessary to supplement these general statistics by individual statistics so that it may be determined whether it is the direct or indirect influence of heat on the organism that is concerned or whether the injury follows from a decomposition of the food. Meyer therefore studied the infants in the orphan asylums of Berlin and also orphans who are cared for outside. They are under constant observation in the so-called convalescent care. These convalescents must be brought to the physician of the asylum every week for examination and exact records are kept. The place in which they are cared for is also inspected every four weeks by a physician, and in the hot months twice weekly by a well-instructed female assistant. There were this year, during the three hot months, June, July and August, 255 children in this convalescent class. The number of nurslings observed in the hospitals amounted to 170 a day. The hospital and outside care supplement each other so that the children may be transferred from one to the other. The temperature during the summer of 1911 was abnormally hot for Berlin. The maximum temperature for June was 85, for July 95 and for August 94 F°. There were seven days in June, ten in July and twenty-three in August in which the temperature exceeded 77 F°. In the previous year there were fourteen days in June, three in July and only two in August with the same maximum temperature. It is known that summer heat depresses adults leading to diminishing of appetite and a lessened intake of nourishment so that there is a certain condition of hunger or fasting with diminished nutrition. The nurslings, on the other hand, are rather more abundantly fed than usual because of the increased thirst. If the infant only shows a loss in the regular increase in weight this must be explained not in the same way as in the adults but must be considered an injury to the function of nutrition itself. This was shown during the hot months. During July and August, 1911, the average was about one-half of the increase for the corresponding months of the previous year. In July, 1910, it was 590 gm.; in July, 1911, 290 gm.; in August, 1910, 600 gm.; in August, 1911, 350 gm. This is a showing that must be brought into immediate relation with the heat. How far the loss may be accounted for by sweating is unsettled. It is only a step from this depressive action on the general condition to a decided pathogenic action. The health of children is incomparably better in the winter months than in the summer and the types of disease vary distinctly.

	Winter 1911		Summer 1910		Summer 1911	
	Cases	Per cent.	Cases	Per cent.	Cases	Per cent.
Nutritional Diseases .....	7	17	21	41	32	34
Furunculosis, Abscess, etc. ..	3	6	16	31	26	28
Respiratory Diseases .....	34	71	12	23	17	18

These figures show first the marked increase in disturbances of nutrition in the hot months and what is certainly not commonly known, a considerable increase in the infections of the skin. Furunculosis, abscess and phlegmon are the immediate results of heat; for by the collection of sweat and the production of decomposition, injuries and inflammations of the skin are produced, which are more serious on account of the decreased resistance occasioned by the heat and the injurious actions of these infections, especially in the young, is reflected in the secondary disturbances of nutrition. One group of diseases noted in 1911 seemed to be due to results of heat stroke. This amounted to 4.2 per cent. of the morbidity, or 1.5 per cent. of the children observed took sick with symptoms similar to heat stroke. Subacute or chronic forms of diarrhea without increase in temperature were lacking in the winter material but are found in the summer proportionally to the prevailing heat. In contrast to the action of heat stroke these disturbances began insidiously and selected ill-nourished children in whom the regular increase in weight had been lacking for weeks previously. During 1910, only rarely was a reduction of the weight observed but in 1911 the reduction went hand in hand with the exaggeration of the entire clinical picture both in the pure alimentary affections as well as in the parenteral affections. Those cases presenting a combination of infectious and alimentary affections had an exceedingly unfavorable course.

Meyer discusses the question as to whether these results are due to decomposition or to diminution of tolerance and says that the insidious nature of the origin of the gastro-intestinal diseases and the aggravation of the clinical picture by heat appear to indicate a diminution of tolerance somewhat in the sense of a diminution of the secretory action of the glands, but this conclusion is not at all definite. Especial care is required in this conclusion as indicated by the observations in the hospitals, where no influence of the heat on the children could be determined, as the increase in weight of the hospital children as in the case of those outside, became smaller. The average monthly increase of all that have been in the institution for fourteen days, including also those in the out-patient service, amounted in June to 400 gm., in July to 320 gm. and in August to 264 gm., and neither overheating, nor increased gastro-intestinal affections, which would indicate an action of heat on the children, were found. As in all institutions the children were loosely clad and their thirst was satisfied by administration of water without any limit. A series of cases of diarrhea occurred but these could be traced to the bad quality of the buttermilk used. Meyer says that putting all of these observations together we must define the influence of heat as follows: The heat acts 1. as an immediate injury to the children by hyperthermia; 2. as a mediate injury by (a) diminution of tolerance, (b) diminution of immunity; (c) by aggravation of the course of the alimentary and infectious diseases; (d) by decomposition of milk.

## INDEX OF CURRENT PEDIATRIC LITERATURE

### ANATOMY, PHYSIOLOGY AND HYGIENE

- Initiation of School Medical Inspection in Queensland. E. E. Bourne.  
Australasian Med. Gaz., September, 1911.
- Hygiene in Home and School. E. Hopkins.  
Kentucky Med. Jour., October, 1911.
- Importance of Medical Inspection of Schools and Its Present Status. J. W. Welch.  
Kentucky Med. Jour., October, 1911.
- Open-Air Schools and Fresh Air in Schools. L. G. Ager.  
Arch. Pediat., October, 1911.
- Relations Between Size of Chest and Skull and the Weight in Infants. (Beziehungen zwischen Brustwachstum, Schädelwachstum und Körpergewichtszunahme bei Säuglingen). E. Zeltner.  
Jahrb. f. Kinderh., October, 1911.
- School Sanitation. D. O. Hancock.  
Kentucky Med. Jour., October, 1911.
- Tentative Classification of Exceptional Children. M. P. E. Groszmann.  
Cal. State Jour. Med., October, 1911.
- Summer Heat and Other Factors in Infantile Mortality. (Einfluss der Hitze auf die Sterblichkeit der Säuglinge.) H. Liefmann and A. Lindemann.  
Med. Klin., Oct. 15, 1911.
- Supply of Iron in the Liver at Birth. (Sulla distribuzione del ferro nel fegato del bambini.) A. Filia.  
Gazz. d. osp., Oct. 15, 1911.
- Secretion in Infant's Breasts as Index of Capacity for Lacteal Secretion in Mother. (Die Brustdrüsensekretion des Kindes als Masstab der Stillfähigkeit der Mutter.) K. Basch.  
München. med. Wehnschr., Oct. 24, 1911.
- Prophylaxis During Childhood. W. B. Hoag.  
Arch. Pediat., November, 1911.
- Infant Morbidity and Measures for Infant Welfare in Chili. (Ueber Säuglingskrankheiten in Chile.) A. Commentz.  
Jahrb. f. Kinderh., November, 1911.
- Photometer for Use of School Physicians. N. B. Harman.  
Brit. Med. Jour., Nov. 4, 1911.
- Infant Mortality and Morbidity in Summer of 1911. (Die Mortalität und die Morbidität der Säuglinge im Sommer 1911.) L. F. Meyer.  
Deutsch. med. Wehnschr., Nov. 9, 1911.
- The Factors Concerned in Milk Secretion.  
Editorial, Jour. Am. Med. Assn., Nov. 18, 1911.
- Influence of Milk Station Work on Reduction of Infant Mortality. G. R. Pisek.  
New York Med. Jour., Nov. 25, 1911.
- Principles of Reduction of Infant Mortality. S. J. Baker.  
New York Med. Jour., Nov. 25, 1911.
- Report on Methods of School Ventilation by the Chicago Commission on Ventilation.  
Jour. Am. Med. Assn., Nov. 25, 1911.
- Report of Committee on Medical Inspection of Schools.  
Jour. Am. Med. Assn., Nov. 25, 1911.

Report of Committee on Administration Methods of Physical Examination of School Children.

Jour. Am. Med. Assn., Nov. 25, 1911.

Training of Nursery Maids in the United States. C. G. Kerley.

New York Med. Jour., Dec. 9, 1911.

Determination of Age of Fetus. (Die Altersbestimmung des Fötus nach graphischer Methode.) W. Zangemeister.

Ztschr. f. Geburtsh., 1911, lxi, No. 1.

Hygiene for Children's Walking Tours. (Die hygienischen Gesichtspunkte für die Veranstaltung mehrtägiger Jugendwanderungen.) H. Roeder.

Arch. f. Kinderh., 1911, lvi, Nos. 4-6.

### PATHOLOGY AND BACTERIOLOGY

Congenital Color Blindness. G. H. Taylor.

Australasian Med. Gaz., September, 1911.

Congenital Amyotonia. (Maladie d'Oppenheim). L. Guinon and Gauducheau.

Bull. de la Soc. de pédiat., October, 1911.

Cancer in the Thymus. (Eine bösartige Thymusgeschwulst.) S. Rubaschow.

Virchow's Arch. f. path. Anat., October, 1911.

Thyroid Changes in Purpura in the New-Born. (Eigentümliche herdförmige Degenerationen der Thyreoidea-Epithelien bei Purpura eines Neonatus.) C. A. Pettavel.

Virchow's Arch. f. path. Anat., October, 1911.

Some Obstructions to Speech Development. G. Hudson-Makuen.

Laryngoscope, October, 1911.

Edemas Occurring Without Albuminuria in Infancy. D. J. M. Miller.

Jour. Med. Sc. of New Jersey, October, 1911.

Fibrous Otitis in Children. (Otitis fibrosa im Kindesalter.) P. Frangenheim.

Beitr. z. klin. Chir., October, 1911.

Involution of Thymus by Roentgen Ray. A. Friedlander.

Arch. Pediat., October, 1911.

A Case of Bacillus Coli Infection Treated Medically, Surgically and Hypnotically. J. Boyd.

Australasian Med. Gaz., October, 1911.

United Twins or Girl with Two Spines Living Till Puberty. (Ueber einen Pantopagus.) J. Linke.

Med. klin., Oct. 15, 1911.

Vasoneurotic Syndromes in Children. (Ueber den vasoneurotischen Symptomenkomplex bei Kindern.) F. Hamburger.

München. med. Wchnschr., Oct. 17, 1911.

Recognition of Congenital Visceral Ptosis in the Treatment of the Badly Poised and Poorly Nourished Child. J. E. Goldthwait and L. T. Brown.

Am. Jour. Orthop. Surg., November, 1911.

A Résumé of the Literature on Sarcoma in Infancy and Early Childhood. Q. W. Hunter.

Pediatrics, November, 1911.

Diseased Children. J. N. Hurty.

Denver Med. Times and Utah Med. Jour., November, 1911.

Methods of Collection, Transmission and Record in Routine Examination of Spinal Fluid. A. J. Chesley.

Jour. Am. Pub. Health Assn., November, 1911.

Pathologic Anatomy and Origin of Tetany in Children. (A proposito di un caso di tetania infantile.) A. Longo.

Policlinico, November, Med. Section, 1911.

Preconceptional Intra-Uterine and Congenital Factors in the Production of Handicapped Children. L. Kerr.

New York State Jour., November, 1911.

- Parathyroid Glands, with Special Reference to Infantile Tetany. R. W. Bliss.  
Arch. Pediat., November, 1911.
- Case of Diabetes Mellitus in a Child Under One Year of Age. P. J. Eaton and E. B. Woods.  
Arch. Pediat., November, 1911.
- Noma. Report of a Case Treated with Salvarsan. M. Nicoll.  
Arch. Pediat., November, 1911.
- Congenital Myatonia; Report of a Case with Autopsy. W. T. Councilman and C. H. Dunn.  
Am. Jour. Diseases of Children, November, 1911.
- Congenital Obliteration of Bile-Ducts. C. P. Howard, and S. B. Wolbach.  
Arch. Int. Med., November, 1911.
- Percussion Signs of Persistent or Enlarged Thymus. T. R. Boggs.  
Arch. Int. Med., November, 1911.
- Hereditary and Familial Splenomegaly. (Zur Kasuistik der heredofamiliären Splenomegalie.) Z. Bychowski.  
Wien. klin. Wchnschr., Nov. 2, 1911.
- Two Cases of Sarcoma of Thymus. W. Sheen, C. A. Griffiths and H. A. Schölberg.  
Lancet, London, Nov. 4, 1911.
- "Comforter" Caries. E. H. R. Harries.  
Lancet, London, Nov. 11, 1911.
- Spasm of the Glottis as Sole Manifestation of Tetany. (Spasme de la glotte; manifestation unique de tétanie.) H. Triboulet and Harvier.  
Ann. de méd. et chir. inf., Nov. 15, 1911.
- Salt Edema in Children without Heart or Kidney Disease. (Ueber Sälzodeme bei älteren Kindern.) F. Hamburger.  
München. med. Wchnschr., Nov. 21, 1911.
- Congenital Elevation of Scapula; Sprengel's Deformity. A. Mitchell.  
Brit. Med. Jour., Nov. 25, 1911.
- Ataxic Type of Infantile Paralysis. J. T. Batte.  
Lancet-Clinic, Dec. 2, 1911.
- Diabetes in Two Infants. (Zusammenstellung zweier pathologisch-anatomisch untersuchter und ganz verschiedenartiger Fälle von Glycosurie mit einigen daran geknüpften Bemerkungen über das Verhalten des Pankreas bei Neugeborenen.) K. A. Heiberg.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Familial Jaundice in New-Born Infants. (Beitrag zum habituellen Icterus gravis der Neugeborenen.) C. May.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Participation of the Sympathetic Nervous System in the Pathology of Infants. (Anteilnahme des sympathetischen Nervensystems an den Erkrankungen des Säuglings.) N. Berend and E. Tezner.  
Monatschr. f. Kinderh., 1911, x, No. 7.

#### METABOLISM AND NUTRITION

- Milk in Its Relation to Health of Infants. H. E. Tuley.  
Jour. Tenn. State Med. Assn., June, 1911.
- Weight of Children Before and After Sanatorium Treatment. (Résultats pondéraux de la cure marine de Giens.) R. Rendu.  
Lyon méd., Oct. 8, 1911.
- Feeding of Infants. E. I. Spriggs.  
Clinical Jour., Oct. 25 and Nov. 1, 1911.
- Further Observations on the Soy Bean. J. Ruhräh.  
Arch. Pediat., October, 1911.
- Sugars in Infant Feeding with Special Reference to Maltose-Dextrin Preparations. J. S. Leopold.  
Arch. Pediat., October, 1911.

- Investigation of Action of Sodium Benzoate in Artificially Fed Infants. C. G. Grulee and W. H. Buhlig.  
Arch. Pediat., October, 1911.
- Some Points to be considered in Feeding Infants. L. Porter.  
Cal. State Jour. Med., October and November, 1911.
- The Feeding of Sick Infants. C. A. Goodrich.  
Yale Med. Jour., October, 1911.
- Importance in Infant Feeding of Proper Balance of Fat and Lime in the Intestines. (Bedingungen für das Zustandekommen fester Stühle beim Säugling.) K. Stolte.  
Jahrb. f. Kinderh., October, 1911.
- Importance of Salts in Breast Milk. (Massgebende Rolle der Salze der Frauenmilch bei der Ernährung in Säuglings- und ersten Kindesalter.) H. Friedenthal.  
München. med. Wchnschr., Nov. 7, 1911.
- Physiologic Lack of Lime in Breast-Fed Infants. (Die physiologische Bedeutung des Kalkhungers bei Brustkindern im ersten Lebensjahre.) W. Dibbelt.  
Berl. klin. Wchnschr., Nov. 13, 1911.
- Viscosity of Human Milk. (Einige viskosimetrische Beobachtungen an der Milch des Menschen.) K. Basch.  
Wien. klin. Wchnschr., Nov. 16, 1911.
- Use of Whole Milk and Fat-Diminished Milk in Infant Feeding. E. A. Darling.  
Boston Med. and Surg. Jour., Nov. 16, 1911.
- Caloric Needs of Premature Infants. J. H. Hess.  
Am. Jour. Dis. Child., November, 1911.
- Use of Malt Sugar and High Percentages of Casein in Infant Feeding. J. L. Morse.  
Am. Jour. Dis. Child., November, 1911.
- Proper Feeding of Infants. C. H. Rice.  
New Orleans Med. and Surg. Jour., November, 1911.
- Case of Infantile Scurvy Due to Sterilized Milk. W. R. Jordan.  
Brit. Jour. Child Dis., November, 1911.
- Can Pure Milk Be Obtained in Portland? C. S. White.  
Northwest Med., November, 1911.
- Iron in Infant Feeding. (Das Eisen bei der natürlichen und künstlichen Ernährung des Säuglings.) L. Langstein.  
Jahrb. f. Kinderh., November, 1911.
- Modification of Cow's Milk. E. J. Labbee.  
Northwest Med., November, 1911.
- Lime Content of Breast Milk and Lack of Lime as Cause of Rachitis. (Der Kalkgehalt der Frauenmilch. Zur Frage der ungenügenden Kalkzufuhr als Ursache der Rachitis.) J. A. Schabad.  
Jahrb. f. Kinderh., November, 1911.
- An Apparatus for the Collection of the Excreta of Infants. E. F. Du Bois.  
Am. Jour. Dis. Child., December, 1911.
- A Metabolism Bed for Infants. J. Howland, and R. A. Cooke.  
Am. Jour. Dis. Child., December, 1911.
- Infant Feeding. (Zur Physiologie und Pathologie der Säuglingsernährung.) A. O. Karnitsky.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Research on Biology of Milk. (Untersuchungen zur Biologie der Milch mittels der anaphylaktischen Methode.) Heubner.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Hemolytic Property of Milk. (Ueber Milchkämolyse.) B. Schmidt.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.

- Training to Increase the Supply of Milk in Wet-Nurses. (Zur Leistungsfähigkeit der Brustdrüse der Ammen.) J. Laurentius.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Lime Metabolism in Rachitis. (Kalkstoffwechsel bei Rachitis.) A. Orgler.  
Monatschr. f. Kinderh., 1911, x, No. 7.

# DISEASES OF THE NEWLY BORN

- Case of Hemorrhage from Stomach in Newly-Born. M. D. Nesbitt.  
Australasian Med. Gaz., September, 1911.
- Congenital Hypertrophic Stenosis of the Pylorus. Report of Case. E. F. Katzmann.  
Kentucky Med. Jour., Sept. 15, 1911.
- Influences During Pregnancy on Unborn Child. J. M. Tompkins.  
Old Dominion Jour. Med. and Surg., October, 1911.
- Resuscitation of Still-Born. Sir F. Champneys.  
Brit. Med. Jour., Oct. 31, 1911.
- Treatment of Obstetric Indentation of the Skull. (Meine Behandlung der Schädelimpression des Neugeborenen.) A. Hoffmann.  
Med. klin., Nov. 12, 1911.
- United Twins: Pygopagus. (Fall von Lebenden zusammengewachsenen Zwillingen—Pygopagen mit bes. Berücksichtigung der operativen Trennung.) P. Bockenheimer.  
Berlin. klin. Wehnschr., Nov. 27, 1911.
- Familial Jaundice in New-Born Infants. (Beitrag zum habituellen Icterus gravis der Neugeborenen.) C. May.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.

# ACUTE INFECTIOUS DISEASES

- Atypical Scarlet Fever. J. P. MacDonald.  
Western Med. Review, September, 1911.
- Epidemic Poliomyelitis in Brazil. (La poliomyélite a Sao-Paulo.) C. Ferreira.  
Bull. de la Soc. pediat., October, 1911.
- The Heart in Scarlet Fever. (Scharlachherz.) R. Lederer and K. Stolte.  
Jahrb. f. Kinderh., October, 1911.
- Decompressive Trephining for Cerebrospinal Meningitis. (Ménigite cérébro-spinale prolongée à forme cachectisante. Syndrome d'hypertension intracranienne. Pronostic fatal. Guérison par une craniectomie décompressive. Double névrite optique par stase.) R. Debré.  
Bull. de la Soc. de pédiat., October, 1911.
- The Pulse Curve in Typhoid in Children. (Ergebnisse kardiosphymographischer Untersuchungen beim Typhus abdominalis im Kindesalter.) W. Schlieps.  
Jahrb. f. Kinderh., October, 1911.
- Scarlet Fever in Apes. (Essais de transmission de la scarlatine aux singes.) K. Landsteiner, C. Levaditi and E. Prasek.  
Ann. de l'Inst. Pasteur, October, 1911.
- Hereditary Transmission of Experimental Relapsing Fever. (L'hérédo-contagion des spirilloles.) L. Nattan-Larrier.  
Ann. de l'Inst. Pasteur, October, 1911.
- Diphtheritic Paralysis. A. Love.  
Glasgow Med. Jour., October, 1911.
- Anterior Poliomyelitis. D. C. Walt.  
Jour. Arkansas Med. Soc., October, 1911.
- Use of Flexner Serum in Cerebrospinal Meningitis. A. E. Cox.  
Jour. Arkansas Med. Soc., October, 1911.
- Cerebrospinal Meningitis. A. L. Carmichael.  
Jour. Arkansas Med. Soc., October, 1911.

- Acute Rheumatism Among Children. F. Langmead.  
Lancet, London, Oct. 21, 1911.
- Anaphylaxis in the Evolution of Infectious Diseases. (De l'anaphylaxie dans l'évolution des maladies infectieuses.) P. Courmont and A. Dufourt.  
Presse méd., Oct. 21, 1911.
- Sepsis After Chicken-Pox. (Fall von Streptokokkensepsis mit purulentem Oedem nach Varizellen.) K. Blühdorn.  
München. med. Wehnschr., Oct. 24, 1911.
- Epidemic Anterior Poliomyelitis: Its Symptoms and Treatment. N. P. Marsh.  
Med. Press and Circ., Oct. 25, 1911.
- Etiology of Scarlet Fever. R. W. C. Pierce.  
Lancet, London, Oct. 28, 1911.
- Our Present Knowledge in Regard to Infantile Paralysis. R. T. Taylor, Baltimore.  
Am. Jour. Surg., November, 1911.
- Prevalence of Infantile Paralysis in Missouri. A. O'Reilly.  
Jour. Mo. State Med. Assn., November, 1911.
- Epidemic Cerebrospinal Meningitis in Children at Athens and Serotherapy. A. Papapanaglotu.  
Arch. de méd. des enf., November, 1911.
- Diphtheria Toxin and Antitoxin in Light of Colloid Chemistry. (Difteritoxin og antitoxin i lyset af kolloidkemien.) M. v. Krogh.  
Norsk Mag. f. Lægevidensk., November, 1911.
- Butyric Acid Test for Epidemic Poliomyelitis. (La butyro-réaction de Noguchi-Moore dans la poliomyélite antérieure aigue.) M. Leitaö.  
Arch. de méd. des enf., November, 1911.
- Question Blank for Records of Epidemic Poliomyelitis. (Vedørende poliomyeliten.) C. Leegaard.  
Norsk Mag. f. Lægevidensk., November, 1911.
- Nasal Diphtheria. (Etude de la diphtérie nasale chez l'enfant.) M. de Biehler and B. K. Dazkiewicz.  
Arch. de méd. des enf., November, 1911.
- Statistics of Infantile Paralysis. C. A. Hodgetts.  
Canadian Med. Assn. Jour., November, 1911.
- Differential Diagnosis Between the Exanthemata. F. H. Dammasch.  
Northwest Med., November, 1911.
- Chorea and Its Treatment. S. F. A. Charles.  
Dublin Jour. of Med. Sc., November, 1911.
- Treatment of Chorea. W. T. Williamson.  
Northwest Med., November, 1911.
- Specific Antibodies in Scarlet Fever. W. W. Koessler and J. M. Koessler.  
Jour. Inf. Dis., November, 1911.
- Bacteriologic Examination of Lymph-Nodes in Scarlet Fever. J. A. Kolmer.  
Am. Jour. Dis. Child., November, 1911.
- Resumé of Diphtheria Examinations Made in Boston Board of Health Bacteriologic Laboratory. F. H. Slack.  
Jour. Am. Public Health Assn., November, 1911.
- Methods of Collection, Transmission and Record in Routine Examination of Spinal Fluids. A. J. Chesley.  
Jour. Am. Pub. Health Assn., November, 1911.
- Search for Causative Factor of Scarlet Fever. M. Nicoll.  
Arch. Pediat., November, 1911.
- Antitoxin in Diphtheria. (Fortschritte in der Behandlung der Diphtherie.) F. Meyer.  
Berlin. klin. Wehnschr., Nov. 6, 1911.
- Case of Antenatal Pneumonia. A. T. I. Macdonald.  
Brit. Med. Jour., Nov. 11, 1911.



- Cerebrospinal Fluid in Acute Poliomyelitis. J. G. Forbes.  
Lancet, Nov. 18, 1911.
- Epidemic Poliomyelitis. Eleventh Note: Relation of the Virus to the Tonsils, Blood and Cerebrospinal Fluids; Races of the Virus. Simon Flexner and Paul F. Clark.  
Jour. Am. Med. Assn., Nov. 18, 1911.
- Scarlet Fever in Apes. Editorial.  
Jour. Am. Med. Assn., Nov. 25, 1911.
- Infantile Paralysis with Especial Reference to Its Occurrence in Massachusetts, 1907-1910. Robert W. Lovett.  
Am. Jour. Dis. Child., December, 1911.
- Ataxic Type of Infantile Paralysis. J. T. Batte.  
Lancet-Clinic, Dec. 2, 1911.
- Epidemic Paralysis (Polio-encephalomyelitis.) S. C. Hounsfield.  
Brit. Med. Jour., Dec. 2, 1911.
- Experimental Measles in the Monkey with Special Reference to the Leukocytes. Ludvig Hektoen and H. E. Eggers.  
Jour. Am. Med. Assn., Dec. 2, 1911.
- Nomenclature of Poliomyelitis (Acute Infectious Paralysis). B. M. Randolph.  
New York Med. Jour., Dec. 9, 1911.
- Vaccination Against Scarlet Fever. (Zur Frage über die Scharlachvaccination und Anginen.) G. E. Wladimiroff.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Eye Complications with Epidemic Meningitis. (Complications oculaires à la suite de méningite cérébro-spinale épidémique. Sérothérapie.) E. Anargyros.  
Grèce Médicale, 1911, xiii, Nos. 13-14.
- Swelling of Glands in Axilla, Neck and Groin as Premonitory Sign of Acute Infectious Diseases. (Ueber ein prämonitorisches Zeichen für die Diagnose von acuter Infektionskrankheit.) G. de G. Giuinta.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Septic Disease in Children. (Zu den septischen Erkrankungsformen im kindlichen Alter.) A. Baginsky.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Influenzal Pyothorax. (Fall von Pyothorax verursacht durch Micrococcus catarrhalis und Influenzabacillen.) M. Lateiner.  
Monatschr. f. Kinderh., 1911, x, No. 7.

#### TUBERCULOSIS AND SYPHILIS

- Research on Hereditary Transmission of Experimental Tuberculosis. Etude expérimentale de l'hérédité tuberculeuse.) L. Landouzy and L. Laederich.  
Presse méd., Oct. 18, 1911.
- Great Reliability of the Pirquet Cutaneous Tuberculin Test for Young Children. (Sur l'utilisation clinique des réactions à la tuberculine chez l'enfant.) M. Péhu.  
Lyon méd., Nov. 5, 1911.
- Relations Between Human and Bovine Tuberculosis. (Der Bericht der englischen Tuberkulose-Kommission über die Beziehungen zwischen menschlicher und tierischer Tuberkulose.) B. Möllers.  
Berl. klin. Wehnschr., Nov. 20, 1911.
- Prenatal and Infantile Tubercular Predispositions. J. B. Huber.  
Am. Jour. Med. Sc., November, 1911.
- Should a Tuberculous Mother Nurse Her Child? M. MacLachlan.  
Northwest Medicine, November, 1911.
- Specific Diagnosis of Tuberculosis in Children. R. W. Matson.  
Northwest Medicine, November, 1911.
- Effect of Salvarsan on Congenital Lues. L. R. DeBuys.  
Arch. Pediat., November, 1911.

- Syphilis in Infancy and Early Life. G. K. Varden.  
 Atlanta Jour.-Rec. of Med., November, 1911.
- Tuberculin as a Diagnostic and Therapeutic Agent in the Treatment of Conjunctivitis Eczematosa. Based on the Study of Fifty Cases. Richard J. Tivnen.  
 Jour. Am. Med. Assn., Dec. 9, 1911.

#### DIGESTIVE SYSTEM

- Case of Hemorrhage from Stomach in Newly-Born. M. D. Nesbitt.  
 Australasian Med. Gaz., September, 1911.
- Congenital Hypertrophic Stenosis of the Pylorus. Report of Case. E. F. Katzmann.  
 Kentucky Med. Jour., Sept. 15, 1911.
- Symptomatic Importance of Constipation in Children. (Valeur séméiologique de la constipation chez les enfants.) E. Périer and Gaujoux.  
 Ann. de méd. et chir. inf., October, 1911.
- Intestinal Invagination in Infant. (Invagination intestinale à marche subaigue chez un enfant de 5 mois  $\frac{1}{2}$ .) Guinon and Fauquez.  
 Bull. de la Soc. de pédiat., October, 1911.
- Colon Irrigation. The Short vs. Long Tube. Comparison Based on 200 Irrigations. H. T. Machell.  
 Arch. Pediat., October, 1911.
- Enteritis in Infants and Its Dietetic Treatment. H. D. Newkirk.  
 Pediatrics, November, 1911.
- Intestinal Infantilism of Herter. R. G. Freeman.  
 Am. Jour. Dis. of Child., November, 1911.
- Ileo-Ileocolic Intussusception Due to Adenoma of Ileum in Child Five Years of Age; Resection of Twelve Inches of Gangrenous Intestine; Recovery. M. S. Kakels.  
 Am. Jour. Surg., November, 1911.
- Noma. Report of a Case Treated with Salvarsan. M. Nicoll.  
 Arch. Pediat., November, 1911.
- Intestinal Worms in Examination of 122 Children. N. Evans.  
 Southern Med. Jour., November, 1911.
- Intestinal Diseases in Infants. J. B. Bilderback.  
 Northwest Med., November, 1911.
- Congenital Intestinal Occlusion. C. A. Wilcox.  
 Jour. Med. Assn. Georgia, November, 1911.
- Saline Infusion in Cholera Infantum. (Zur Therapie vorgeschrittenster Fälle von Sommerdiarrhœ bei Säuglingen.) W. Löbisch.  
 Wien klin. Wehnschr., Nov. 23, 1911.
- Use of Hypertonic Salines Controlled by Estimation of Specific Gravity of Blood in Infantile Diarrhea. L. Rogers.  
 Brit. Med. Jour., Nov. 25, 1911.
- Treatment of Habitual Vomiting in Infants. (Le traitement des vomissements habituels des nourissons.) L. Cheinisse.  
 Semaine méd., Nov. 29, 1911.
- Pyloric Stenosis in Older Children with Report of a Case of Pyloric Spasm Ending Fatally. E. E. Graham.  
 Am. Jour. Dis. Child., December, 1911.
- Treatment of Diarrheas in Bottle-Fed Infants. R. H. Dennett.  
 Med. Rec., New York, Dec. 2, 1911.
- Congenital Megalocolon and Anal Atresia. H. B. Sheffield.  
 Med. Rec., New York, Dec. 9, 1911.
- Prevalence of Helminthiasis in Children. (Studien über die Häufigkeit der Darmparasiten, namentlich des Oxyuris vermicularis, bei Kindern.) A. Routsalainen.  
 Monatschr. f. Kinderh., 1911, x, No. 7.

**RESPIRATORY SYSTEM**

- Asthma in Children.** (L'asthme chez les enfants.) J. Comby.  
Arch. des méd. des Enfants, October, 1911.
- Pneumohypoderma (Emphysema Cutis). Scleredema Neonatorum.** H. B. Sheffield.  
Med. Rec., New York, Nov. 25, 1911.

**BLOOD AND CIRCULATORY SYSTEM**

- Mikulicz' Disease, with Report of Case of Lymphatic Leukemia in Child with Marked Enlargement of Salivary Glands.** W. Tileston.  
Am. Jour. Dis. Child., November, 1911.
- Hereditary and Familial Splenomegaly.** (Zur Kasuistik der heredofamiliären Splenomegalie.) Z. Bychowski.  
Wien. klin. Wchnsch., Nov. 2, 1911.
- Acute Myeloid Leukemia.** (Akute myeloische Leukämie.) C. Sternberg.  
Wien. klin. Wchnsch., Nov. 23, 1911.
- Management of Heart in Acute Infectious Diseases and Chronic Heart Diseases.** E. G. Cutler.  
Boston Med. and Surg. Jour., Dec. 7, 1911.
- Action of Pilocarpin on the Blood.** (Einwirkung von Pilocarpin auf das Blut, insbes. auf die Eosinophilen.) S. Aschenheim and Tomono.  
Monatschr. f. Kinderh., 1911, x, No. 7.
- Physiologic Fluctuations in Refracting Power and Viscosity of Infants' Blood.** (Die physiologische Schwankungen der Refraktion und der Viskosität des Säuglingsblutes.) Reuss.  
Monatschr. f. Kinderh., 1911, x, No. 7.
- The Blood with Jaundice in the New-Born.** (Zur Lehre des Icterus neonatorum.) F. Heimann.  
Ztschr. f. Geburtsh., 1911, lxi, No. 1.

**NERVOUS SYSTEM**

- Congenital Spastic Paralysis.** (Om Behandlingen af Morbus Little.) H. Scheuermann.  
Hospitaltidende, Sept. 27, 1911.
- Dull and Backward Children.** A. F. Tredgold.  
Brit. Jour. Chil. Dis., October, 1911.
- Feeble-Minded Children.** (Ueber der kindlichen Schwachsinn, seine Symptomatologie, Diagnose und Therapie.) J. Raecke.  
Deutsch. med. Wchnsch., Oct. 12, 1911.
- Congenital Spastic Paralysis.** (La maladie de Little. Etiologie, pathogénie et anatomie pathologique.) V. Hutinel and L. Babonneix.  
Ann. de méd. et chir. inf., Oct. 15, 1911.
- Neuro-Functional Disturbances in Children and Best Treatment to Prevent and Correct Resultant Deformities.** J. W. Cokenower.  
Med. Fortnightly, Oct. 25, 1911.
- Chvostek's Sign and Neuropathies in the Young.** (Fazialisphänomen und jugendliche Neuropathie.)  
Wien. klin. Wchnsch., Oct. 26, 1911.
- The Medical Examination of Children Reported as Mentally Defective in the Public Schools.** I. T. Smart and M. S. Macy.  
Pediatrics, November, 1911.
- Some Causes and Prevention of Insanity and Feeble-Mindedness.** J. W. Graves,  
Northwest Med., November, 1911.
- Mental Training in Childhood.** R. Jones.  
West. Canada Med. Jour., November, 1911.
- Dementia Præcox and Scientific Research.** B. Holmes.  
Med. Fortnightly, Nov. 10, 1911.

- Spasm of the Glottis as Sole Manifestation of Tetany. (Spasme de la glotte; manifestation unique de tétanie.) H. Triboulet and Harvier.  
Ann. de méd. et chir. inf., Nov. 15, 1911.
- Nature and Treatment of Painful Paralysis of the Arm in Children. (Zur Auffassung und Therapie der schmerzhaften Armlähmung der Kinder. Dérangement interne des Unterarms.) E. Durlach.  
Berl. klin. Wehnschr., Nov. 20, 1911.
- A Motor Neurosis Probably Responsible for Rumination in Infants. (Zur Pathogenese der Rumination im Säuglingsalter.) F. Leist.  
Monatschr. f. Kinderh., 1911, x, No. 6.

#### GENITO-URINARY SYSTEM

- Polyp of Urinary Bladder in Thirteen Months' Old Child. I. S. Koll.  
Ann. Surg., November, 1911.
- Acetonuria in Childhood. R. S. Frew.  
Lancet, London, Nov. 4, 1911.
- Color Reaction in Breast-Fed Infants' Urine. (Zur Engel-Turnau'schen Harnreaktion.) E. Langfeldt.  
Berl. klin. Wehnschr., Nov. 20, 1911.
- Tube-Casts in Urine. Sur Pathologie der Zylindrurie.) J. Peiser.  
Monatschr. f. Kinderh., 1911, x, No. 7.

#### SKIN AND APPENDAGES

- Management of Infantile Eczema. A. J. Markley.  
Pediatrics, November, 1911.

#### EYE, EAR, NOSE AND THROAT

- Congenital Color Blindness. G. H. Taylor.  
Australasian Med. Gaz., September, 1911.
- Treatment of Adenoids and Diseases of the Tonsils. W. W. Carter.  
Long Island Med. Jour., September, 1911.
- Radical Removal of Tonsils and Adenoids. C. G. Kerley.  
Arch. Pediat., October, 1911.
- Tonsillectomy. W. G. Shadrach.  
New Mexico Med. Jour., October, 1911.
- Juvenile Hydrophthalmos. (Hydrophthalmus infantiles.) J. Fejer.  
Berl. klin. Wehnschr., Oct. 16, 1911.
- Individual Ampuolas with Silver Nitrate for the Eyes of the New-Born. (Weitere Erfahrungen mit meiner Methode der Credéisierung.) H. Hellendall.  
Zentralbl. f. Gynäk., Oct. 21, 1911.
- Postnasal Catarrh in Children and Its Consequences. E. Smith.  
Lancet, London, Oct. 28, 1911.
- Syllabus for Lectures to Medical Students on Deaf Child. G. Hudson-Makuen.  
Laryngoscope, November, 1911.
- A General Consideration of the Tonsil Operation. A. J. Hill and G. F. Zinninger.  
Ohio State Med. Jour., November, 1911.
- Classification of Deaf Children. M. Yearsley.  
Brit. Jour. of Child. Dis., November, 1911.
- Nitrous Oxid Anesthesia in Adenoid and Tonsil Operations. C. A. Gundelach.  
Interstate Med. Jour., November, 1911.
- Removal of Tonsils as Prophylactic Measure. H. H. Forbes.  
Am. Medicine, November, 1911.
- Steam Treatment of Acute Gonorrheal Conjunctivitis. (Neue Behandlungsmethode der akuten gonorrhöischen Konjunktival blenorrhoe.) W. Goldzieher.  
Wien. klin. Wehnschr., Nov. 23, 1911.

- Enucleation of Tonsils with Guillotine. S. S. Whillis and F. C. Pybus.  
 Brit. Med. Jour., Nov. 25, 1911.  
 Strabismus in infants and young Children. I. M. Heller.  
 Med. Rec., New York, Dec. 9, 1911.

### SURGERY

- Treatment of Scoliosis in Childhood. A. H. Tubby.  
 Med. Press and Circ., Nov. 1, 1911.  
 Surgical Operative Steps in Closure of Cleft Palate. G. V. I. Brown.  
 Jour. Ophth. and Oto-Laryngol., November, 1911.  
 Operative Treatment of Congenital Wry Neck. J. K. Young.  
 Am. Jour. Orthop. Surg., November, 1911.  
 Results of Muscle Group Isolation in Treatment of the Paralyzes of the Extremities. N. Allison and S. I. Schwab.  
 Am. Jour. Orthop. Surg., November, 1911.  
 Operation for Cleft Palate After Infancy. L. Emerson.  
 Jour. Med. Sc. New Jersey, November, 1911.  
 Surgical Treatment of Anterior Poliomyelitis. A. M. Forbes.  
 Canadian Med. Assn. Jour., November, 1911.  
 Wedge Incision in Treatment of Rachitic Curvature of the Leg; Two Cases. (Les incurvations rachitiques de la jambe et leur traitement chirurgical.) V. Veau.  
 Arch. de méd. des enf., October, 1911.  
 Treatment of Rachitic Curvature of the Legs. F. Hohmeier.  
 Deutsch. med. Wehnschr., Oct. 19, 1911.  
 Treatment of Hypospadias in Children. (Hypospadias pénien chez l'enfant.) M. Ombrédanne.  
 Presse méd., Oct. 21, 1911.  
 Results of the Manipulative Treatment of Congenital Dislocation of Hip-Joint. G. C. E. Simpson.  
 Lancet, London, Oct. 21, 1911.  
 Eclampsia Complicating Labor in Girl Aged 12; Recovery of Mother and Child. C. H. Roberts.  
 Brit. Med. Jour., Oct. 21, 1911.  
 Care of Stump of Umbilical Cord. (Abnabelung und Nabelschnurversorgung.) F. Ahlfeld.  
 Zentralbl. f. Gynäk., Oct. 28, 1911.  
 Further Series of Eighty-One Consecutive Cases of Cleft Palate Treated by Operation. J. Berry.  
 Brit. Med. Jour., Oct. 28, 1911.  
 Orthopedic and Operative Treatment of Little's Disease. (Traitement orthopédique et chirurgical de la maladie de Little.) A. Broca.  
 Ann. de méd. et chir. inf., Nov. 15, 1911.  
 Treatment of Cleft Palate. Sir H. Butlin.  
 Lancet, London, Nov. 25, 1911.

### MISCELLANEOUS

- Pediatrics in 1910. E. Terrien.  
 Med. Press and Circ., Oct. 25, 1911.  
 Dull and Backward Children. A. F. Tredgold.  
 Brit. Jour. Child. Dis., October, 1911.  
 Infant Morbidity and Mortality in Summer of 1911. (Die Morbidität und die Mortalität der Säuglinge im Sommer 1911.) L. F. Meyer.  
 Deutsch. med. Wehnschr., Nov. 9, 1911.  
 Reasons for State Care of the Crippled and Deformed; Problems Involved. H. W. Orr.  
 Am. Jour. Orthop. Surg., November, 1911.

- Recent Developments in the Care of Adolescent Weak Back. W. Truslow.  
Am. Jour. Obst. and Dis. of Women and Child., November, 1911.
- Some Symptoms in Childhood. J. B. Barrett.  
Dublin Jour. of Med. Sc., November, 1911.
- The Child as an Asset to the Nation. A. M. Paterson.  
Pediatrics, November, 1911.
- Infant Morbidity and Measures for Infant Welfare in Chili. (Ueber Säuglingskrankheiten in Chile.) A. Commentz.  
Jahrb. f. Kinderh., November, 1911.
- Functions of a State Pediatric Society. H. L. Coit.  
Arch. Pediat., November, 1911.
- Teaching of Pediatrics at the University of Stockholm. (Die Pädiatrie als Unterricht- und Prüfungsfach an dem Karolinischen medico-chirurgischen Institut zu Stockholm.) O. Medin.  
Jahrb. f. Kinderh., November, 1911.
- Duty of the Country Physician to the Mother and Child. H. C. Curtis.  
Jour. Tenn. State Med. Assn., November, 1911.
- The Need of Care for Crippled Children. D. C. McMurtrie.  
West. Canada Med. Jour., November, 1911.
- Tentative Classification of Exceptional Children. M. P. E. Groszmann.  
Cal. State Jour. Med., November, 1911.
- Case of Diabetes Mellitus in a Child One Year of Age. P. J. Eaton and E. B. Woods.  
Arch. Pediat., November, 1911.
- The Copenhagen Institution for Cripples. Its History, Work and Results. D. C. McMurtrie.  
Boston Med. and Surg. Jour., Nov. 25, 1911.
- Children's Hospitals with Infant Wards. (Ueber Bau und Einrichtung von Kinderkrankenhäuser, mit Säuglingsabteilungen vom Standpunkt der öffentlichen Gesundheitspflege.) A. Franz.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.
- Diabetes in Two Infants. (Zusammenstellung zweier pathologisch-anatomisch untersuchter und ganz verschiedenartiger Fälle von Glycosurie mit einigen daran geknüpften Bemerkungen über das Verhalten des Pankreas bei Neugeborenen.) K. A. Heiberg.  
Arch. f. Kinderh., 1911, lvi, Nos. 4-6.

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## THE POLYGRAPH AS AN AID IN DIAGNOSIS OF CARDIAC CONDITIONS IN CHILDREN \*

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NEW YORK

That there has been no startling advance in our methods of physical diagnosis since the days of Skoda and his pupils will probably not be denied. These men left us a rich heritage, and we are only now, through the use of scientific instruments, blazing new paths and adding valuable record findings to those of the unaided senses.

The use of the polygraph with adults has proved of great value in correlating physiologic and clinical data. It has removed that element which we speak of as the "personal equation," and instead gives records which are true for all time, and only require correct interpretation. These records have stimulated closer study of the heart and the circulation, so that the anatomist, physiologist, pathologist and clinician have all profited thereby and developed newer conceptions of the intricate cardiac mechanism.

The studies of Gaskell, who showed that the heart muscle itself possesses characteristic tone, that it can originate its own stimulus and conduct it to various parts of the heart, explained many of the phenomena recorded in polygraphic tracings. For example, the physiologist now knows that the auricle contracts an appreciable, measurable interval before the ventricle, and that the stimulus which produces cardiac contraction arises at the mouths of the great veins, spreading down successively over the right auricle, thence through the bundle of His and its branches to the ventricles.

Further, it has been shown that a dissociation between auricle and ventricle can be produced experimentally by destroying the tissue at the auriculo-ventricular junction, which contains special muscle and nerve fibers, and which seems to be a "connecting pathway" for the contraction stimulus.

With the polygraph we can show definitely whether the cardiac rhythm is normal; if normal, whether the arrhythmia is due to respir-

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\*Read before the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

atory or other influences; whether ventricular contraction follows auricular contraction as it should; whether the excitability of the heart is normal. With this instrument it is possible to study the function of the cardiac muscle, namely, tonicity, rhythmicity, contractibility and conductivity. Thus far, the function of conductivity is best understood, and we find it disturbed in the usual forms of pulse irregularity. A study of the polygraphic tracings tells whether the irregularity is due to heart block, fibrillation of the auricle, or extra-systole, and, if the latter, which one of the three varieties of extra-systole is present. All these facts are of the greatest importance, for we have at hand by this means, in certain cases, just as precise knowledge (of the cardiac function) as one obtains by finding the malarial parasite in the blood-cells.

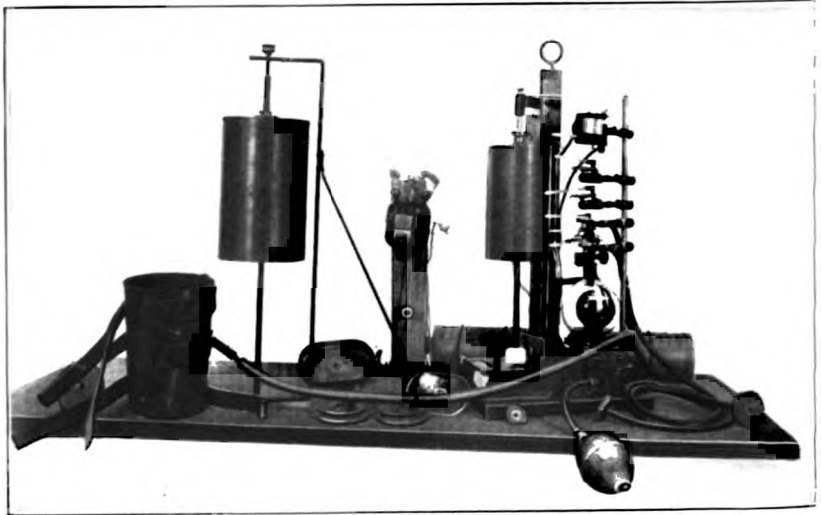


Fig. 1.—Modified Sphygmograph. With this instrument long tracings may be taken of brachial artery, apex, respiration, jugular vein and time (in  $1/10$  second).

With these facts in mind, we undertook the application of these methods in cardiac conditions in children, to determine (1) if satisfactory tracings could be made from children; (2) if information additional to that obtained in the physical examination was possible; (3) if this information could be utilized in prognosis and treatment.

The instrument used in our work was our modification of the Erlanger sphygmograph with a Hirschfelder attachment (Fig. 1). This apparatus allows a simultaneous tracing to be made (1) of the pulse — known as the sphygmogram; (2) of the heart — cardiogram; (3) of the venous pulse — phlebogram. These three tracings, when studied in



relation to each other, become much more valuable than when taken alone, even with the finest instrument.

The sphygmogram gives information relating to the movements of the left heart, the rate and rhythm of the heart, and the variations in pressure within the artery.

The cardiogram gives the tracings made over the precordium, or apex, and gives exact data concerning the heart movements, and aids in defining the cardiac systole. It should not be forgotten that the cardiogram does not record the pressure within the ventricle, but does give information as to the displacement of the heart in relation to the chest wall. It further indicates certain physiologic events which are



Fig. 2.—The Normal Phlebogram (Hay). Diagram from actual tracings showing the variations in the records of the auricular type of venous pulse. The upper phlebogram is normal, the lowest shows the marked effect of free tricuspid regurgitation in increasing the engorgement of the right auricle. Note the gradual increase of the wave *v* at the expense of the auricular depression *x*. The portion *v'* of the ventricular wave *v* occurs in the phlebogram before the perpendicular line 5.

helpful in determining pathologic states of the heart. In other words, the cardiogram gives information regarding the duration of the systole and diastole, the beginning of ventricular systole, and indicates the period of the action of the aortic valves and the opening of both cuspid valves. Sometimes the normal type of cardiogram becomes inverted—where there is such marked hypertrophy and dilatation of the right ventricle as to force the left ventricle out of position on the chest wall. How valuable such information may be to the clinician need not be

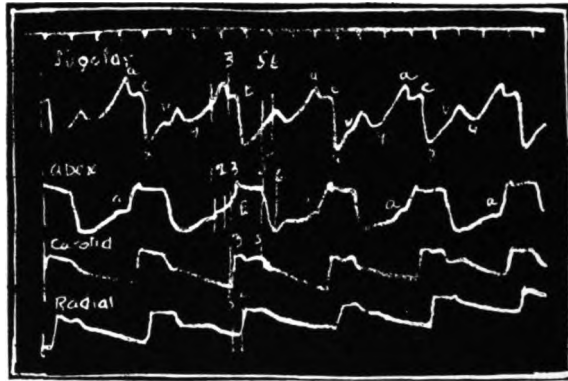


Fig. 3.—Normal tracings from jugular vein, apex, carotid and radial arteries recorded simultaneously (Mackenzie). The line above the jugular tracing is the time in  $1/5$  second. Note the waves, *a*, *c* and *v*. The beginning of the wave *c* occurs just  $1/10$  second before the rise (due to ventricular systole) in the radial as shown in line 3 in radial and jugular tracings. The *a* wave, due to auricular systole, begins about  $1/5$  second before *c* as shown by line 1, in the jugular tracing. This is during the diastole of the ventricle as shown by the falling line in the radial tracing at this time. The beginning of the wave *v*, occurs usually at the beginning of the rise in the radial. Its fall, however, marks the opening of the auriculo-ventricular valves and is coincident with the dicrotic notch of the radial tracing. The jugular pulse varies considerably, but the waves *a*, *c* and *v* can be measured off as has been explained.

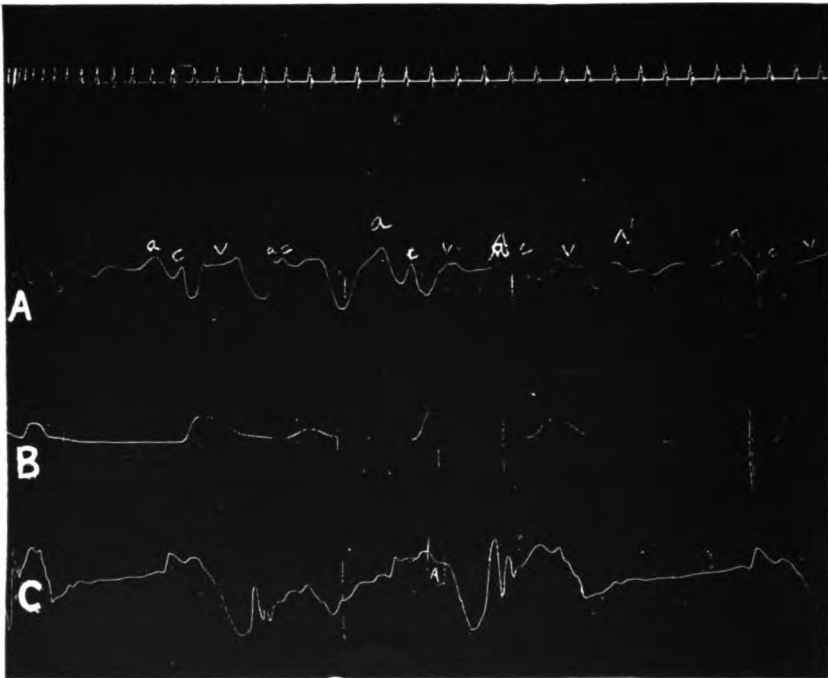


Fig. 4.—Digitalis heart-block, in a boy 15 years old. After stopping digitalis the heart-rate became normal. At *A'* in the jugular tracing is evidence of auricular contraction, while there is no contraction of the ventricle. A, right jugular, B, brachial, C, apex curves.

emphasized here, since he may be able to note on subsequent records in convalescence the gradual return of the left ventricle to its place, as shown by a positive cardiogram.

The phlebogram is of these three records the most important, as by representing the variations in venous pressure (when taken in the neck),

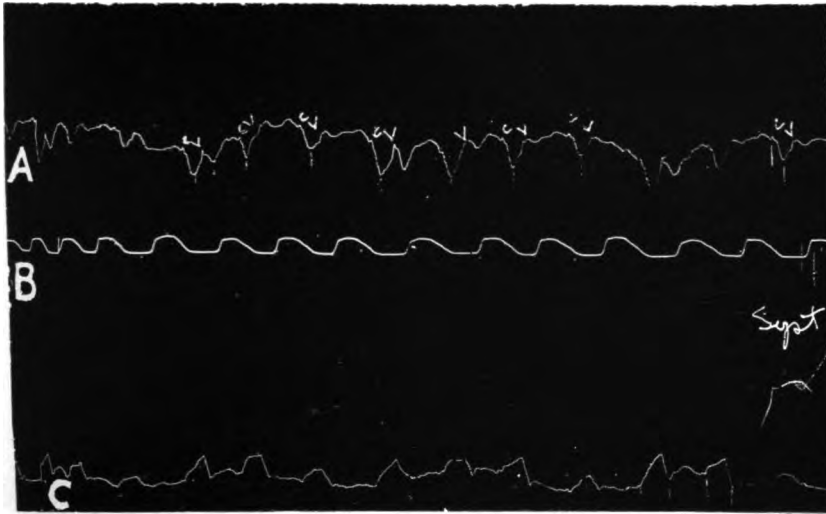


Fig. 5.—M. M., aged 10 years; respiratory arrhythmia; mitral insufficiency. Large jugular tracing, third heart sound. "H" wave in jugular. A, right jugular, B, brachial, C, apex curves.

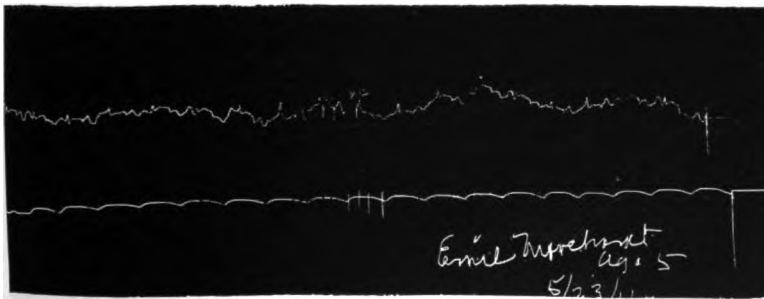


Fig. 6.—E. M., aged 15 years; normal heart; respiratory arrhythmia. Note the large jugular waves in upper tracing.

it indicates the activities of the right side of the heart. While in some instances the interpretation of these tracings has led to controversial theories, in the main observers agree, and at all events the records stand ready for any advance in this field of medicine.

In reply to the first problem which we undertook to answer: Can tracings be obtained satisfactorily from children? In our series of cases,

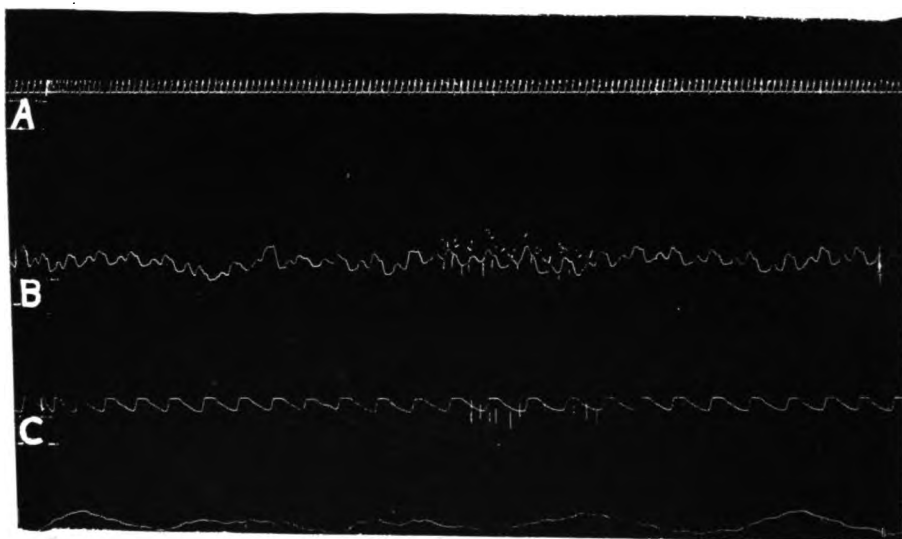


Fig. 7.—B. W., aged  $4\frac{1}{2}$  years. Congenital pulmonary stenosis. Note the large jugular waves. A. time, 0.1 second; B, right jugular, C. brachial curves.

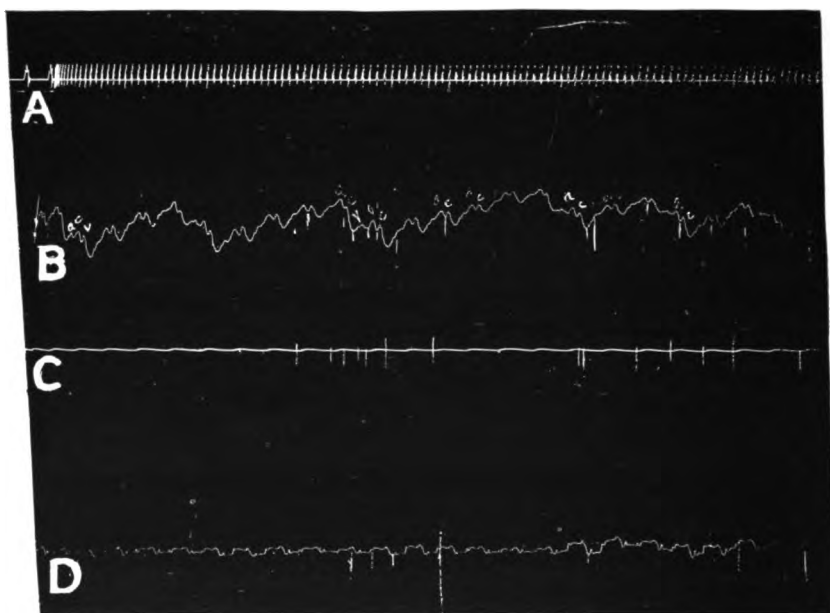


Fig. 8.—M. K., aged 5. Mitral insufficiency—uncompensated. Note large jugular waves and protodiastolic wave in cardiogram (associated with "third heart sound"). A. time 0.1 second; B. right jugular, C. brachial, D. apex curves.

the ages of the children varied from  $4\frac{1}{2}$  to 15 years, and all were suffering from cardiac lesions, either congenital or acquired. In each case we obtained satisfactory tracings from the brachial artery, precordium and the jugular bulb. With only slight modification of the appliances to suit the smaller anatomical areas we were able to make records without difficulty. For examples of well-marked jugular tracings in children see Figures 5 to 14 inclusive.

Before taking up the second question, or the value of tracings taken in children, it may be well to review briefly the anatomic and physiologic essentials on which interpretations are made.

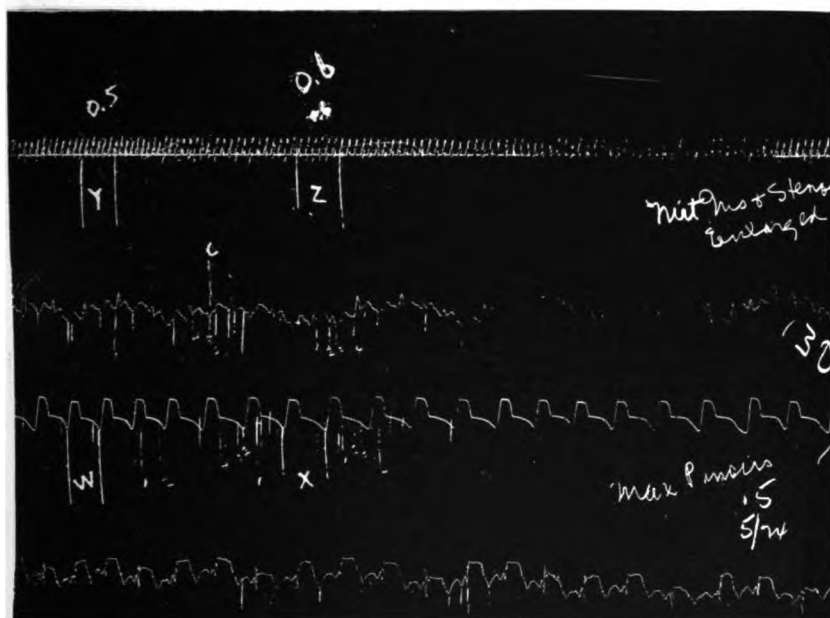


Fig. 9.—M. P., aged 5. Mitral insufficiency and stenosis; cardiac enlargement. Note respiration effect on cardiac rhythm; increased frequency with inspiration, decreased with expiration. Cardiac cycle W. 0.5 sec., cycle X—0.6 sec. Note protodiastolic wave "p" in cardiogram (associated with third heart sound) and corresponding wave "h" in jugular.

The right jugular bulb, which is found to be about one inch outside of the sterno-clavicular articulation, is the point over which the cup is placed to obtain the venous tracing. The right internal jugular, innominate vein, and superior vena cava, extend almost in a straight line from the heart. The pulsations are best obtained by lowering the child's head and placing it in such a position that there is a relaxation of the sterno-cleido-mastoid muscle. The best point to obtain the tracing from the jugular vein is about three-quarters to one inch external to the right sterno-clavicular articulation.

The normal venous tracing shows three distinct waves, called the (a), (c) and (v) waves (Figs. 2 and 3). The (a) wave occurs early in diastole of the ventricle, as can be seen by placing the hand over the apex and watching the time of this rise in the jugular pulse. The wave, however, is the result of the auricular contraction.

Following the (a) wave, a negative phase is recorded, termed (x), caused in greater part by the diastole of the ventricles, but this is interrupted by the (c) wave which is synchronous with the carotid pulsation.

The "a-c interval" is almost constant in point of duration, i. e., one-fifth of a second in the normal heart — and indicates the time of passage

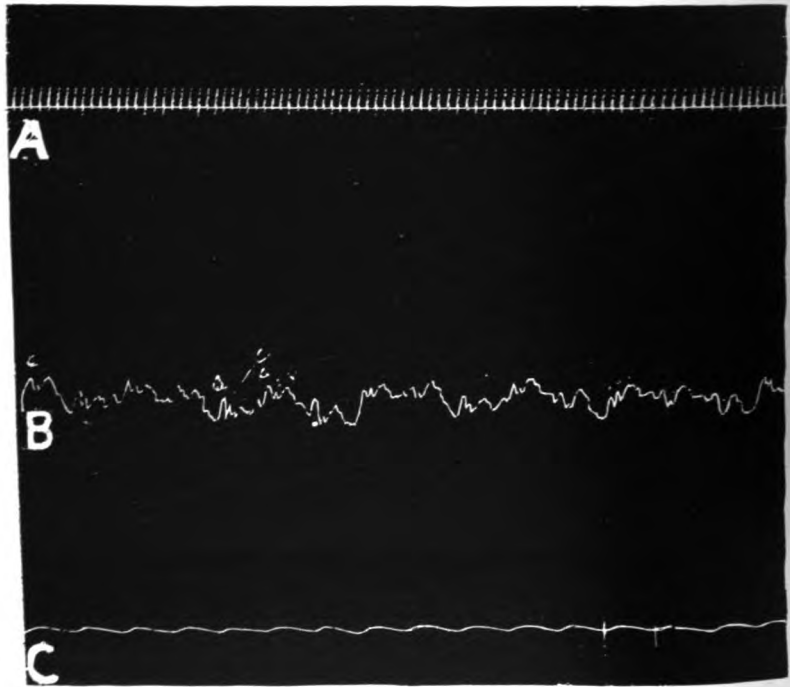


Fig. 10.—T. S., aged 7 years. Mitral insufficiency—uncompensated. Note the large jugular waves (B). A, time 0.1 second, B, right jugular, C, brachial curves.

of the contraction stimulus through the "conducting pathway" (Bundle of His).

The third wave (v) occurs synchronously with the systole of the ventricle. It is increased in size by any factors which tend to more rapidly fill the right auricle, and hence the veins.

A second negative diastolic phase (y) follows the (v) wave and records the emptying of the cervical veins. The importance of noting this wave is seen in cases of engorged right heart with over-distended veins in the neck. In these instances it is found practically absent.

To analyze a tracing from the jugular vein, one must compare it with a tracing taken at the same time from the brachial or radial artery (see Fig. 2). With a pair of compasses, place the left point on the first vertical or base line in the radial tracing; place the other point at the beginning of any rise; then move back the right leg of the compass one-tenth of a second, as indicated on the timer above; then place the left leg on the base line of the jugular, and the right point will fall on the beginning of the rise of the (c) wave. This should be the time for (c) in the jugular tracing, for it occurs one-tenth of a second earlier in the jugular than in the radial. Then measure one-fifth of a second to the left of this (a) wave, which should fall on "a." The wave following (c) is (v).

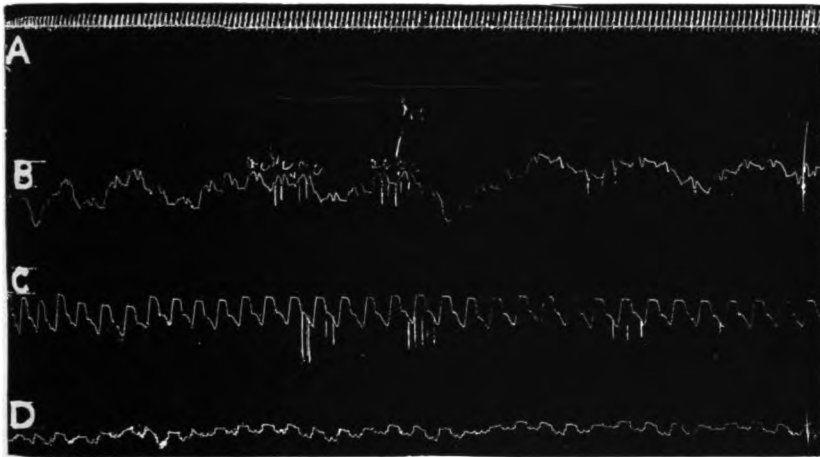


Fig. 11.—L. B., aged 12 years. Neurotic heart. Note character of jugular and cardiac tracings. A well-defined "p" is present in the cardiogram, with an occasional "h" wave in the jugular tracing. A, time 0.1 second; B, right jugular, C, brachial. D, apex.

In interpreting any polygraphic tracing, it is advisable to consider the functions of cardiac muscle, particularly that of conductivity. Cases of Stokes-Adams disease have recently been reported in adolescents, and undoubtedly cases of partial heart-block occur with severe cardiac lesions.

Normally, the a-c interval is of short duration. If the function of conductivity is interfered with, then the passage of the stimulus through the auriculo-ventricular bundle (or bundle of His) is delayed, causing the a-c interval to be lengthened. This form of cardiac arrhythmia is found in acute ulcerative endocarditis, and not infrequently in cases of heart-block which have come to necropsy actual destruction of the bundle of His has been found.

If the lesion in this auriculo-ventricular bundle is so extensive as to cause complete "blocking" of the stimulus, then ventricular contraction does not follow that of the auricle, as it normally should, resulting in what is known as "heart-block." The dissociation between auricle and ventricle may be absolutely complete (the auricle beating independently of the ventricle and vice versa) or the ventricle may beat to every second, third or fourth auricular contraction.

Digitalis is often indiscriminately prescribed to children because they "have a valvular lesion." The polygraph teaches that it should never be prescribed for any individual whose a-c interval is prolonged, since it then only depresses the function of conductivity and accentuates any arrhythmia which is present. Such an instance from our series is presented in Figure 4. The patient was a boy of 15 admitted to the hospital with marked decompression. He had been taking digitalis in large doses—15 minims of the tincture four times a day. On the seventh day the pulse, which had been regular, showed marked arrhythmia. The tracing, Figure 4, was taken on the eighth day, and shows typical heart block. The digitalis was then stopped, and seven days later his pulse was regular. The cause of such irregularities can best be recognized by the polygraph. Here we have a condition which, if not recognized, may become serious. Ordinary methods of physical examination do not reveal the real condition.

Of the other functions of cardiac muscle, that of stimulus production was found particularly interesting in our series of tracings. In *every case* we found a quickening of the pulse with inspiration and a slowing with expiration. This is known as respiratory arrhythmia (Figs. 9, 5 and 6). That it is caused by irregularly produced stimuli is shown by the fact that ventricular contraction follows auricular contraction normally; in other words, that there is no disturbance of conductivity, an important fact to recognize. The cardiac muscle in neurotic children is particularly predisposed to this disturbance.

No evidences of the function of excitability were noted in our records. This was contrary to our expectations, since the child is apparently susceptible to abnormal or irregular stimuli in other portions of its organism. We concluded, therefore, that the myocardium in the young does not exhibit any extra systoles, even in rapidly beating hearts.

Another point of interest in our study was the occurrence of the "third heart sound." This is accompanied by characteristic waves in the cardiogram and phlebogram (Figs. 5, 8, 9, 10). The significance of this is as follows:

In some cases the existence of this extra heart sound was not noted on the preliminary physical examination, and it was only recognized after its appearance on the tracing had specifically called our attention to its presence. Thayer states that it can be heard at the apex in about



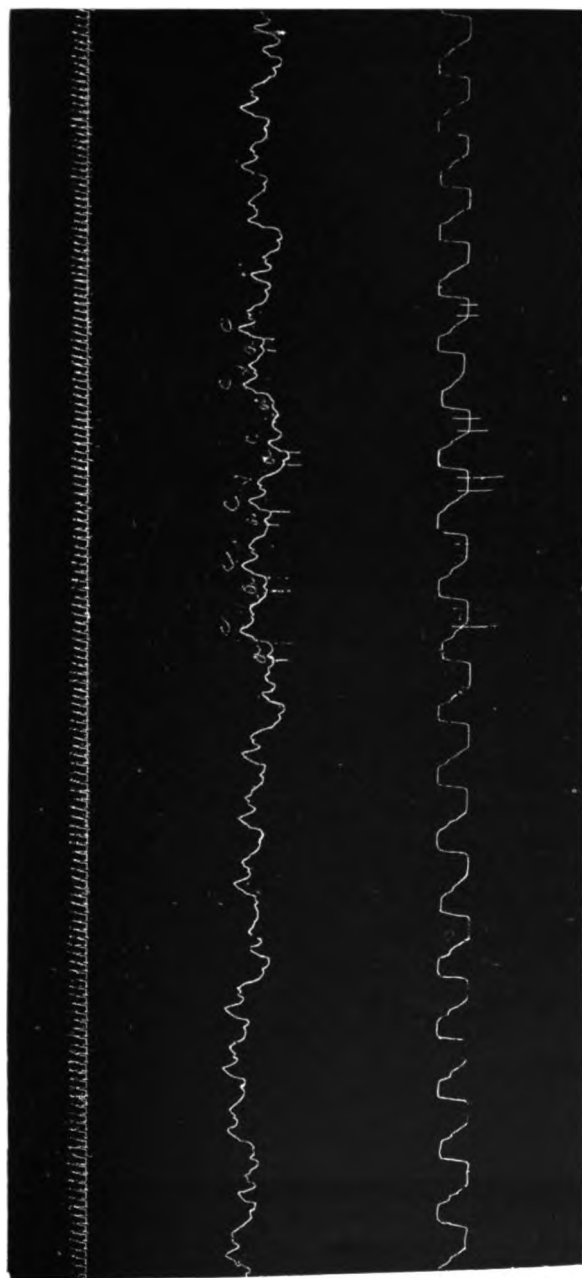


Fig. 12.—G. S., aged 12 years. Mitral stenosis. Note large jugular waves (upper tracing).

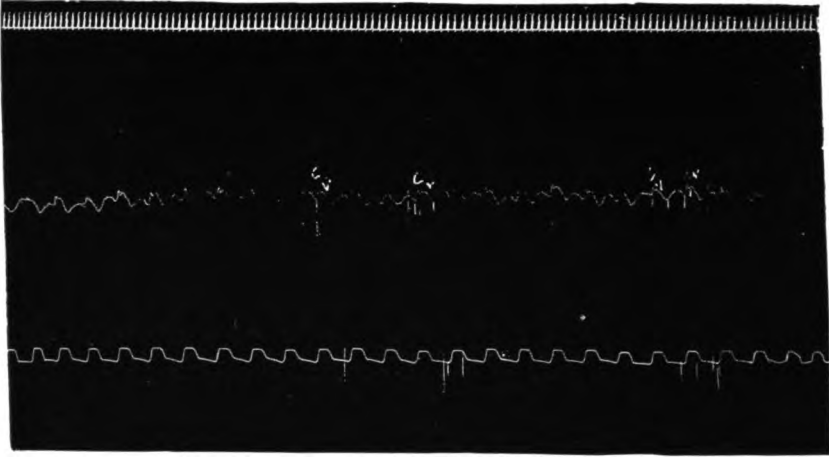


Fig. 13.—E. B., aged 13 years. Mitral insufficiency; overacting heart with slight hypertrophy. Note the excellent jugular tracing with normal *a c v* waves. Auricular type.

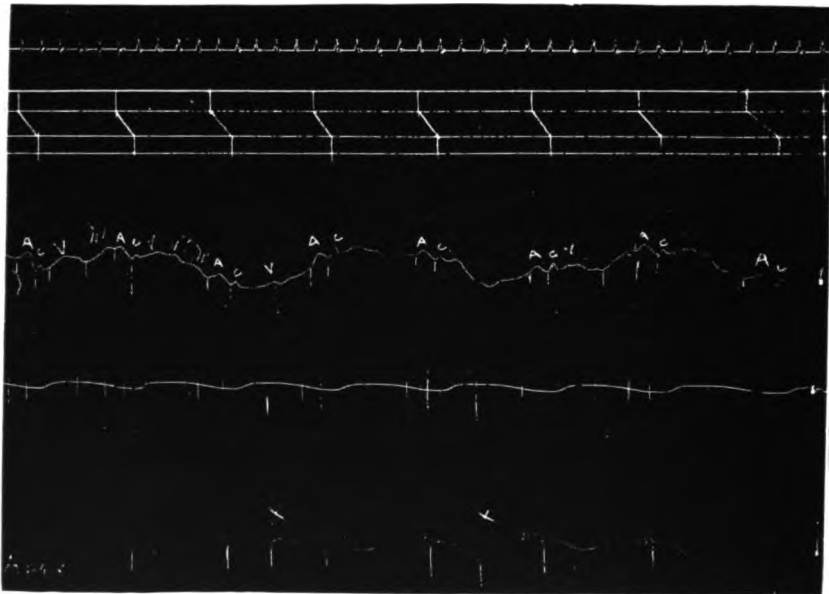


Fig. 14.—T. S., aged 6½ years. Mitral insufficiency and aortic insufficiency. Diagram represents passage of stimuli through auriculo-ventricular bundle. Normal

30 per cent. of normal individuals, when they are lying on the left side. In the first decade it occurs in 58.9 per cent. of cases.

This protodiastolic wave in the cardiogram is associated with an extra wave (h) appearing soon after the (v) wave in the jugular tracing (Figs. 5, 8, 9, 10) and therefore occurs in the early filling of the heart; in other words, at the very beginning of diastole. At this time the mitral and tricuspid valves are closed by the elastic recoil of the heart walls. Hirschfelder believes that it is due to the sudden snapping together of these valves. This wave may be pronounced whenever there is a ventricular distention — as in dilatation following hypertrophy, in stenosis of the mitral valve, and in aortic insufficiency, in which there is found to be an increase of intraventricular pressure. It is always accompanied by a wave designated as "p" on the cardiogram.

#### CONCLUSION

When making a physical examination of a patient with heart disease, perhaps the least important for the patient is the determination of the precise valve involved. The examiner should endeavor to determine the exact power of the heart to respond, to study the functioning ability of the myocardium and obtain data of the cardiac activity. These facts, in conjunction with the physical findings as to size, possible dilatation, or organic lesion, enable the physician to form a much more precise opinion as to the prognosis, while his treatment, at least, is based on scientific facts and can be controlled by further observations.

The results of our study may be summarized as follows:

1. Tracings satisfactory for diagnosis can be obtained in children.
2. The polygraph offers a means of accurate diagnosis which is not afforded by ordinary methods of examination, and should be used in addition to these — it will not replace them.
3. The information obtained from polygraphic tracings is of value for prognosis and treatment. Digitalis heart-block should be suspected where the pulse becomes irregular under the use of this drug.
4. Respiratory arrhythmia was found in our series with surprising frequency. This is said to be physiological, but we are led to suspect that it may frequently be misleading, and that the physician may suspect serious cardiac weakness. This was illustrated in cases of scarlet fever, diphtheria and measles studied by us at the Contagious Hospital. The "irregular hearts" were shown to have marked respiratory arrhythmia. We have yet to find extra systoles or auricular fibrillation in children.

The use of the polygraph will not stultify physical findings: on the contrary, more careful examinations will be made, for its use enhances their value and interprets observations which have thus far been unexplained.

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## THE PHYSICAL EVIDENCE OF THE THYMUS<sup>1</sup>

CARL BASCH, M.D., AND ADOLF ROHN, M.D.

PRAGUE

*Translated by A. C. Soper, Jr., M.D., Chicago*

Recent experimental work in the physiology of the thymus has cleared up matters in two directions, namely, the relation of the organ to growth and to the condition of the bones, on the one hand, and to the electrical excitability of the nervous system, on the other.

When one completely extirpates the thymus of a young dog in the first weeks of life, there occurs as a consequence not only a checking of growth, but a condition in which the bones become softer and more flexible and show a smaller callus after an artificially produced fracture than is seen in a control animal of the same brood. If one tests the electric stimulation of a young dog over the median nerve or the cerebrum, before and after the extirpation of the thymus, one can demonstrate after extirpation a gradually increasing hyperexcitability, which may be raised to the same degree as that produced by extirpation of the "epithelkorperschen." By injection of soluble calcium salts this hyperexcitability can be again reduced to normal.

Originally these experiments were based on an article by Basch<sup>2</sup> read at the Natural Philosophy Convention in Karlsbad in 1902, entitled "Extirpation of the Thymus Gland;" later communications appeared in the *Jahrbuch für Kinderheilkunde*, 1906 and 1908. Naturally these articles met with criticism from various sources, but were completely substantiated.

If we wish to refer to articles demonstrating the relation of the thymus gland to the osseous system, we note the work of Cozzolino<sup>3</sup> and Ugo Soli,<sup>4</sup> that of Lucien and Parisot,<sup>5</sup> of Sommer and Floercken (Würzburg),<sup>6</sup> of Ranzi and Tandler (Wien),<sup>7</sup> and the recent work of Klose and

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1. Originally published in *Deutsch. med. Wehnschr.*, 1911, xxxvii, 1843.

2. Basch, K.: *Wein. klin. Wehnschr.*, 1903, No. 31; *Jahrb. f. Kinderh.*, 1905; and 1908; *Monatschr. f. Kinderh.*, vii; *Ztschr. f. exper. Path. u. Therap.*, 1905; *Lotos*, lvi.

3. Cozzolino: *La Pædiatria*, 1903; *Congresso di Med. Int. Padova*, 1903.

4. Soli, Ugo: *Arch. ital. de biol.*, 1907-9; *Mem. R. Acad. Modena*, 1909; *Poli-clinico*, 1907.

5. Lucien and Parisot: *Arch. d. méd. exper.*, 1910, p. 98.

6. Sommer and Floercken: *Berl. klin. Wehnschr.*, 1908; *Phys. med. Gesellsch., Würzburg*, 1908.

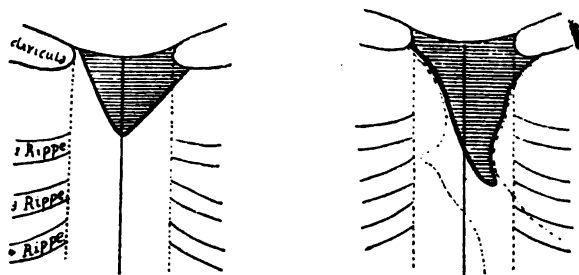
7. Ranzi and Tandler: *Wien klin. Wehnschr.*, 1909, No. 27.

t (Frankfurt)<sup>8</sup> entitled "Clinical and Biological Features of the thymus."

Close and Vogt in their comprehensive research into the extirpation of the thymus in young dogs not only showed the bone changes, but were the first to prove the nerve irritability, and were able to prove undoubted histologic changes as well.

Rebele<sup>9</sup> and Hart and Nordmann<sup>10</sup> in their researches also obtained identical symptoms of loss of function. Among the later workers in the comparative physiology of the thymus only Rudolf Fischl<sup>11</sup> failed to find any effect after thymus extirpation, and came to the conclusion that the thymus has no rôle in extra-uterine life. The negative result of this work is, however, as Basch has shown, due to the fact that the experiments of Fischl were arranged in a faulty manner, and the elementary principles of thymus research neglected.

With the changes mentioned — the change in the development of the thymic system and the increase of nerve excitability in an animal deprived



1 and 2.—Diagrammatic representations of the thymus gland, after Fischl.

of the thymus — depend simply and clearly on a uniform cause — altered metabolism, a point recently demonstrated by Basch<sup>2</sup> and by

Close. The histology of the thymus is intimately connected with the function of the thyroid gland as well as the epithelial cells, with which it is histogenetically connected, and belongs to the same great group of the "branchiogenic organs."

The relation of the thymus to osseous development and to nerve irritability is by no means a specific peculiarity confined to this organ.

What gives the thymus its peculiar difference from the other endocrine glands which have an internal secretion is the fact that its function is

<sup>1</sup> Close and Vogt: Beitr. z. klin. Chir., lxxix.

<sup>2</sup> Basch: Arch. f. klin. Chir., 1910.

<sup>3</sup> Hart and Nordmann: Berl. klin. Wchnschr., 1910, No. 18.

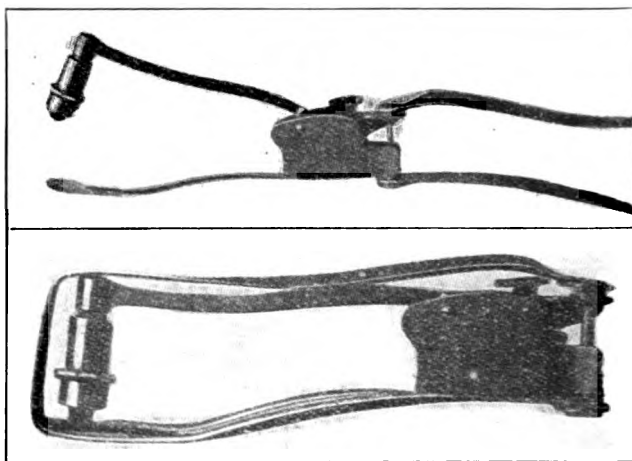
<sup>4</sup> Fischl, Rudolf: Ztschr. f. exper. Path. and Therap., 1905; Monatschr. f.

<sup>5</sup> Rebele: Rev. Clin. Pædiat., 1905.

only transient, and that besides its correlation to the glands with internal secretion, it is to an extraordinary degree related to the lymphoid apparatus of the body; conclusions as to this are possible only after an exhaustive research. When a thorough research into the physiology of the thymus has been taken up, it is to be hoped that especial attention will be given to the differences existing in the living.

To find such a method, or to prepare the way for it, was the first object of our work, and for this purpose the use of the material in the *Franz Josefs Kinderspital* was offered. Robert Blumenreich<sup>13</sup> was engaged in a similar work in 1900, and the results of his work, which we shall next review, were reported in *Virchow's Archives*.

Blumenreich used as material for his work mostly the cadavers of the Berlin Pathological-Anatomical Institute, and made exact drawings from



Figs. 3 and 4.—Specially devised percussion instruments for outlining the thymus.

over fifty-five cases. Following the directions of Sahli, he lightly percussed with the finger the thymic area, drew on the skin the areas of relative and absolute dulness, and marked them internally with blackened needles driven into the chest. Then by dissection he proved the relation of the percussion outline to the actual position of the thymus. Also, in fifteen of his fifty-five cases he had the opportunity to percuss the thymic area both before and after death. Of the fifty-five cases, twenty-two were infants between 1 month and 1 year old; the rest were children up to 9 years.

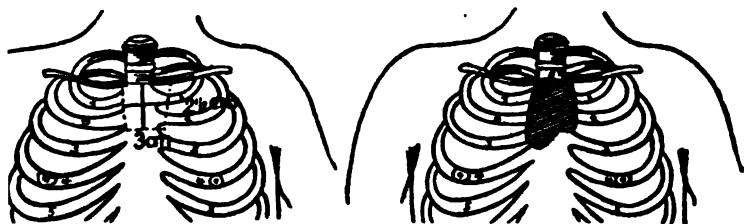
Blumenreich found that up to the end of the fifth year there was an unmi-takable area of dulness over the thymus which in general presented an irregular triangle, whose base was the sterno-lavicular articulation.

13. Blumenreich: *Virchow's Arch. f. path. Anat.*, clv.

whose rounded apex lay at the level of the second rib, or occasionally below it, while the sides reached over the edge of the sternal line. The larger part of the area of dulness lay generally on the left side, and the form of it varied but little within the age limits mentioned. After the sixth year of life the frequency with which dulness was found decreased (Figs. 1 and 2).

When one compares the area of thymic dulness on a living child as drawn by Blumenreich, with the position of it in the cadaver, one sees that by this method the glands bordering on the lungs, as well as the "lingual" lobes of this organ in the living, do not appear to view; and for a complete investigation a research which will also include these parts is necessary.

When one deliberates as to which is the most suitable method to solve this question, one naturally chooses the Roentgen ray in the place, since it possesses an advantage over other methods in being free from the danger of errors. Since Blumenreich's publication of Roentgen ray photography of the thymus has been used very extensively by Holzknacht<sup>14</sup> in 1901, Hochsinger<sup>15</sup> in 1903, and by L. Rehn<sup>16</sup> in 1906.



5 and 6.—Percussion findings (Fig. 5) as compared with autopsy findings (Fig. 6) in a child aged 4 months; necropsy three days after clinical examination.

When, in roentgenizing the anterior thorax, one noted a downward movement of the gland in inspiration and an upward movement on expiration. According to Hochsinger the thymus shadow normally impinges on the lower border of the scapula like the narrow neck of a bottle, and forms a band covering the lower part of the vertebral column. According to Holzknacht a completely developed thymus shows, by sagittal rays, a triangular shadow in the anterior thorax like that of an enormously dilated heart or a pericardial effusion.

He ascribes it to the thymus, whose shadow obscures that of the aorta, the pulmonary vessels and the heart.

On frontal and oblique rays, the usually clear retrosternal space is obscured by the thymus shadow. No Roentgen pictures are given in the

<sup>14</sup>Holzknacht: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1901.

<sup>15</sup>Hochsinger: Wien. klin. Wchnschr., 1903.

<sup>16</sup>L.: Arch. f. klin. Med., 1906.

Desiring to form for ourselves an independent judgment as to whether it is possible to obtain a clear shadow of the thymus in a Roentgen photograph, we prepared photographs of a young dog having a relatively large thymus, before and after extirpation, by means of instantaneous and time exposures, and a lead screen. In order to mark the exact location of the extirpation we sewed up the sternal cut with silver thread; nevertheless we were unable to find in the photographs any marks which could be definitely declared to be thymus shadows.

Next we took instantaneous pictures of an anatomic preparation of the sternum of a young dog, one exposure with thymus attached and another of the sternum alone; we could neither find any sign of a thymus shadow, nor see that the clear picture of the sternum was at all obscured by the underlying thymus.

Also, the thoracic photograph of two young children of the ages of 2 and 6 months gave negative results in respect to thymus shadows. The taking of further pictures induced us to regard the question of the clearness of the thymus shadow as still unsettled, and to speak very reservedly of our ability to give an instantaneous and unmistakable conclusion of the size of the thymus. Perhaps the instantaneous photography of Dessauer has given the progress desired; in an article by Alweus<sup>17</sup> a striking result in this line is seen in the accompanying thorax photographs of a child with pertussis.

But even if the experience with the Roentgen ray had been more satisfactory than was the case, better results would be found in refining and improving the older physical methods of percussion and auscultation of the thymus, since much smaller and simpler apparatus is needed for demonstration, and therefore it can be much more easily used in daily practice.

Since the position of the thymus is much more hidden than that of other large glands, such as the liver or spleen, one must admit, *a priori*, that the differentiation of this organ from its surroundings is much more difficult. Even if it is feasible now to get a more exact idea of the width and length of the thymus by percussion than before, this outlining of its size is to be accepted with caution, since by percussion alone no idea is to be had of an important factor—the thickness of the thymus. But in spite of this fact, we should not cease in our endeavors to perfect this method of estimating the size, since only in this fashion can the clinical foundation of pathologic study of the organ be undertaken.

If one looks for a contrasting problem, take the one of outlining the heart. It, as well as the thymus, is an organ characterized by its being free from air and yet in part overlapped by the air-filled lungs. Yet the heart affords a far easier outline for demarcation by percussion, having

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17. Alweus: München. Wchnschr., 1911, p. 737.

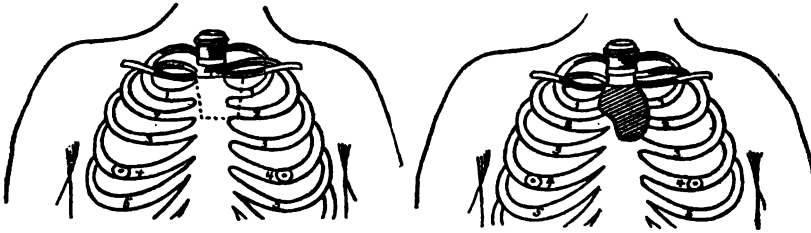


a firmer structure, being filled with fluid, and covered only by the thin ribs and intercostal muscles.

The thymus is covered by the thick sternum and rests on the air-filled trachea, by which any jarring may change the percussion sound, and the thymus edges are almost continuously covered by lung tissue. In emphysema of the lungs, in which the heart is generally more obscured by the dilation of the lungs, and held in a rigid thorax, the percussion more nearly approaches that of the normal thymus.

A short time ago the use of auscultatory percussion for outlining the heart in emphysema was suggested by Bock<sup>18</sup> in Munich, who recommended the use of a specially constructed stethoscope, a procedure which compares very well with the Roentgen-ray outlining.

The method urged by Bock consists in this, that his stethoscope as originally designed permitted a gradual muffling of the sound and was put on the middle of the sternum; the sound was shut off about one-half and the area was percussed by an assistant.



Figs. 7 and 8.—Clinical and necropsy findings in a child 1 year old with chronic nutritional disturbance and subnormal body-weight. Autopsy several months after clinical examination.

According to Bock the person examining with the instrument in the manner directed — shutting off the half — is able to hear those vibrations which are usually lost in the deeper parts of the thorax, while those arising in the superficial parts, such as the edges of the lungs, aid the return of the deep percussion note.

The conventional percussion of the upper thorax with one's finger as recommended by Sahli and Blumenreich,<sup>18</sup> afforded us a too meager result, as the finger seemed too thick an instrument to use on the thorax of an infant, so we invented a little "stockel-plessimeter" for light percussion of the thoracic area, and confined ourselves to auscultatory percussion. In order to make it possible for one person to do this auscultation and percussion, and to make the technic as exact and uniform as possible, Basch constructed an instrument which duplicates the mechanism of the percussing finger but is lighter and can be easily used with one hand. It touches only about a quarter of a centimeter of surface, and can easily be moved across these small areas laterally as well as longitudinally. The

18. Bock, H.: München. med. Wehnschr., 1908, No. 11.

half shut-off stethoscope is held over the mid-sternum with the other hand, and the percussion note heard by the one who makes it.

The use of this new instrument shows that it is possible to obtain a more definite and exact outline of the anterior thoracic organs than by earlier methods such as the finger. In contrast to the triangular area of dulness over the thymus pictured by Blumenreich, we found, by direct and by auscultatory percussion, an area somewhat larger than that which has been before demonstrated. It is probable that the instrument will be found to be of value in general percussion, as with it the cardiac area of a young child with yielding thoracic walls may be easily outlined.

By careful percussion of the anterior thorax with the instrument shown in Figures 3 and 4 the area of absolute thymus dulness is obtained and drawn with a colored pencil on the skin. This drawing we regard as the first sketch of the area of dulness, to be perfected by further examination. In many cases the relative dulness is obtained by auscultatory percussion, especially toward the left side of the thorax. In general the results from the auscultatory percussion agree with those of the precise instrument.

Besides this, we have used a method to outline the lateral areas of the thymus, described by Bianchi and A. Smith<sup>19</sup> a short time ago — the so-called friction method. For we found the original method devised for heart outlining, by which the phonendoscope is set in the area of absolute dulness and the adjacent areas stroked with a brush or the finger, very complicated and not well chosen. The friction method we used in this way:

An open, sound-magnifying phonendoscope was placed in the thymic area, a small bristle brush drawn diagonally over the sternal area, and attention paid to the point where the scraping sound was weakened or deadened. Only in cases in which the thymus extended beyond the sternum could we find a change in the scraping sound — where it seemed to be of considerable thickness; thus a further means of estimating the thymus was found.

A simple physical experiment illustrates the technic of the friction method. If one takes a cardboard box, on the bottom of which a heap of sand is put, and holds it in an oblique position, when the outer side is scratched with a brush one can locate the edge of the sand by the cessation of the scratching sound if this has a depth of only a centimeter. Marking the border found and opening the box at the same angle, one is convinced of the correctness of the marking.

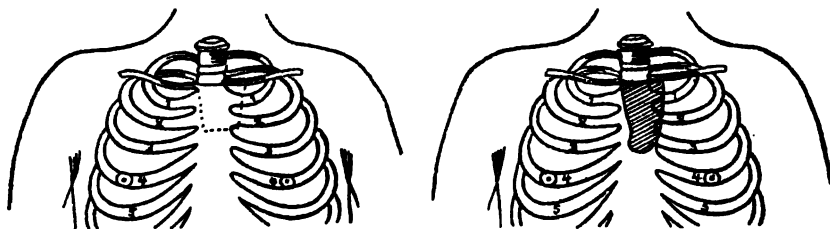
A similar phenomenon is observed in the friction examination of the thymus area. If one lays the open bell of the phonendoscope over the thymus area, first to the left and then to the right, and with a brush strokes the skin in an oblique direction, one hears the transmission of the

19. Smith, A.: (Refers. to Bianchi) *Kongr. f. Inn. Med.*, 1900.

scratching sound as long as the brush is over the air-filled lungs. The sound is deadened or silenced on the spots where lung tissue ends and the thick thymus underlies the sternum. In children under 2 years, in whom the thymus is flat or small, the method is useless, as well as on the cadaver, in which instance the lungs have collapsed.

By this method we examined in the out-patient clinic of the hospital a number of children aged 6 to 18 months, and later up to 3 and 4 years. Beyond the fifth year no sure thymus dulness could be demonstrated. For the greater part of our study we used, as far as possible, well-nourished and developed children with only minor diseases, in order to have a picture of the physiologic condition of the thymus. But we also collected a considerable amount of material for the pathologic study, regarding which we will speak later. A majority of the findings it was possible to prove by autopsy; these were naturally the ones most valuable for instructive deductions.

As a rule each of us worked independently of the other, and drew his findings on a diagram of the anterior thorax. After some preparatory



Figs. 9 and 10.—Clinical findings (Fig. 9) confirmed at necropsy (Fig. 10) in a child 1½ years old, well nourished, dying of descending croup.

trials necessary to make one familiar with the peculiarities of the method, the results obtained were uniform. Usually we took only a few cases each day, because the experiment was conducted with strained attention and therefore produced fatigue. The methodical procedure was the following:

The child, undressed, was first laid on a sofa in a flat position, and a roll put under its neck and shoulders to throw the upper thorax more forward, lifting the chin upward. Then with our percussion instrument, whose surface spanned perhaps a quarter of a centimeter, the anterior thorax was methodically percussed, with the lightest and most uniform strokes, and point by point in exact rows the area to be examined was studied in a lattice work of small squares. The dulness found by direct percussion was marked on the skin with a blue pencil, and next the half-deadened stethoscope of Bock placed in the middle of the sternum and fixed with the left hand, and the thymic area again percussed with our instrument. Alterations shown by auscultatory percussion were drawn on the figure.

Finally the completely opened stethoscope was moved about from right to left below the thymus area, and the thymic area stroked in an oblique direction with a brush. This is especially valuable in the children over 1 year old. The results from this friction method were also noted.

The area of dulness thus mapped out was, as nearly as possible, estimated with reference to the sternum and ribs. It should be carefully noted how far from the median line of the sternum or the parasternal line the lateral borders come. The lower border should be measured with reference to the upper or lower edge of the second or third rib, and drawn in conformity to a diagram of the anterior thorax. Also, the greatest diameter of the dulness should be measured, vertically and horizontally.

The sketches made in this way of the topography and size of the thymus should be compared with the findings from an autopsy of the cases. In the cases we describe here, more than 140 were examined clinically, and one-tenth of these were confirmed by autopsy. We found in the cases examined considerable variations in the size of the thymus dulness. We were able, however, in place of these to use the material chosen for the physiologic data, in which we could find a large group of children of the same age among the well-developed and nourished ones.

It is already known that the thymus shows a constant development with the increasing age of the child, and grows until the age of puberty. Its growth is not uniform, however; its most intense growth is between the second and fifth years of life. It does indeed increase in weight until the fifteenth year, but in relation to the rest of the body is smaller. According to the estimates of v. Sury<sup>20</sup> and the careful examinations of Hammar<sup>21</sup> the thymus weight is reckoned:

	v. Sury gm.	Hammar gm.
In the new-born .....	14.4	13.28
From 1-5 years .....	22.1	22.98
From 6-10 years .....	29.4	26.10
From 11-15 years .....	32.2	37.50

While the thymus weight in the new-born bears a proportion of about 4-1,000 to the rest of the body mass, and in the first to the fifth year about 2.2-1,000, the proportion sinks by the tenth year to 1.2-1,000, and in the fifteenth year to 0.1-1,000.

After puberty a gradual shrinkage of the thymus sets in, a physiologic involution, while during exhausted periods at any age a marked reduction in size can be demonstrated, the so-called accidental involution. Soderlund and Backmann<sup>22</sup> in their animal experiments were able to show

20. Von Sury: Vierteljahrschr., f. gerichtl. Med., 1908.

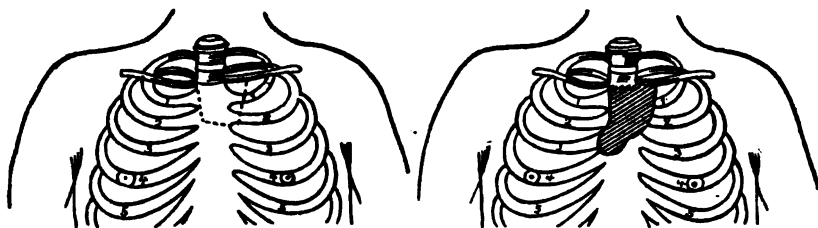
21. Hammar: Arch. f. Anat. u. Physiol., 1906; Vierteljahrschr. f. gerichtl. Med., 1908.

22. Soderlund and Backmann: Arch. f. microscop. Anat., 1909.

a reduction to one-tenth of the thymus weight after several days of starvation.

In general we concluded from the foregoing data that the greatest anatomic development and the most important biologic epoch could be looked for between the second six months and the third year of life, and therefore we selected this period for our physiologic experiments. In contrast to Blumenreich we found in this period a more rhomboid form of thymic dulness whose size and location varied with the age of the child. The lower edge generally reached to the second or third rib, and commonly ran in an oblique direction. And in agreement with Blumenreich and in contradiction of an old declaration of Sahli's, a clear full tone was demonstrable between the lower border of the thymus and the upper border of the heart.

While we try in the following experiments to give the most typical examples in each age classification, at the same time we will preferably regard only such cases as were proved by autopsy. In this way the worth of the physiologic experiments can be best judged. In children in the first half year of life we found the thymic dulness in the form of a small



Figs. 11 and 12.—Thymus findings in a child 4 years old which died of heart disease following diphtheria; size of thymus on dissection corresponded with percussion findings. A small, tongue-shaped lobe extended downward toward the right side, which could not be outlined by percussion.

trapezoid which stretched from the jugular to the second rib; the right border lay mostly in the right sternal line, but more often in the middle line. The left border generally extended over the right sternal line, but was not so sharply defined as the left.

In a case of a 4 months' child brought to autopsy three days after the original examination, the volume of the thymus at section overlapped the dulness area found clinically, as is shown in Figures 5 and 6, and this thymus lay deeper in the thorax than could possibly be ascertained physically.

In a child about 1 year old, with a chronic nutrition disturbance and subnormal body weight, in which the autopsy cited was done several months after the clinical findings were made, the two pictures are contrasted as in Figures 7 and 8. In a child a year and a half old, which had been in a very well-nourished condition and died of an intercurrent infection (descending croup), we outlined on the cadaver the thymus

dulness shown in Figure 9, and confirmed it by autopsy as seen in Figure 10. Here the dulness-area found covered the upper part of the thymus as seen at autopsy, but besides this a tongue-shaped lobe extended down toward the heart (Fig. 10), which lobe was so covered by a thick layer of lung tissue that to find it by percussion could not be expected.

In another case, confirmed at autopsy, a child about 4 years old of fairly good nutrition died of heart disease several weeks after a diphtheritic attack; the size of the thymus when dissected out was exactly that of the area of dulness found by percussion. Here there was also a small tongue-shaped lobe, but it extended toward the right side and forbade physical outlining (Figs. 11 and 12).

The thymus dulness of children between 2 and 3 years — a period we have so far been unable to study by autopsy — does not differ materially from the case of an 18 months child shown in Figure 9.

Thymus dulness may easily be wrongly diagnosed from other features in the mediastinal space.

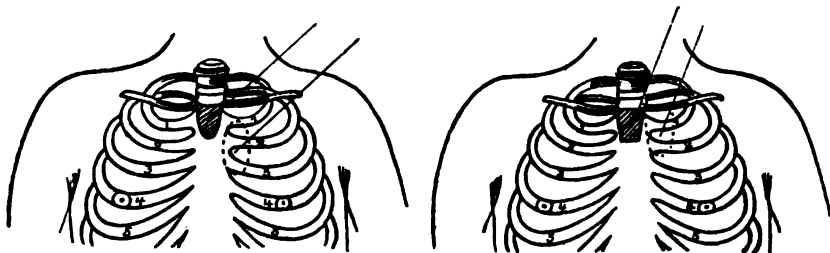


Fig. 13.—The area of atypic dulness outlined a caseous lymph-gland on the left side; thymus in the median line, small, and did not show perceptible dulness.

Fig. 14.—Atypical dulness caused by infiltration of left lung; thymus small and not demonstrable by percussion.

Of the factors which may be mistaken for enlargement of the thymus, the lymph-glands in childhood take first place, whether they are only swollen or are infected with tuberculosis. On the other hand such organs as can cause a dull area in the adult, like a struma or a mediastinal tumor, come under observation only exceptionally in the child, and may be ignored. Next in importance are the changes in the lung parenchyma, whether inflammatory or tuberculous, which, when they cause a dulness in the neighborhood of the thymus in children, cause deception in diagnosing thymus dulness.

In a part of the cases a conclusion may be reached that this dulness is not that of the thymus, because it lies in an atypical place, and does not show the median position of a thymus. Such atypical dulness should be regarded with distrust as not belonging to the thymus. If one finds foci of infiltration over the lungs, or a positive reaction for tuberculosis, one should be inclined to ascribe the dulness rather to the diseased foci. Auscultation will often decide this fact.

But if swollen or caseous lymph-glands lie under the thymus or are even adherent to it, it is almost impossible to differentiate these in the living. We have been able to draw some important conclusions from the autopsies of children we could examine during life, and show such cases in Figures 13, 14 and 15.

In Figure 13 the atypic dulness outlines a caseous lymph-gland on the left side, while the thymus lay in the median line, was very small, and did not show a perceptible dulness.

In Figure 14 a similar atypical dulness is that of an infiltrated left lung, and the thymus was here also very small and not demonstrable by percussion.

In Figure 15 again the caseous lymph-glands lie in the median line and are adherent to the thin thymus and present the picture of an enlarged thymus. Only the fact that a Pirquet reaction was positive in

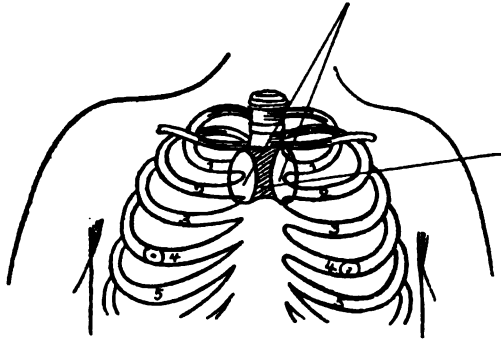


Fig. 15.—Caseous lymph-glands in the median line adherent to the thymus, presenting the picture of an enlarged thymus.

the seventh month, had warned us that we must not ascribe this dulness solely to the thymus.

Among the cases examined so far we found besides the common signs pertaining to the thymus, a certain multiplicity of facts which lead us to believe that we have made a step forward in the knowledge of the condition of the thymus in childhood, and shall make others. On account of the incompleteness of the physical methods, however, we must exert ourselves to find further functional reactions, which will help to broaden the results of physical examination.

#### CONCLUSIONS

Combining an exact percussion of the mediastinal area, which is done with the new percussion instrument, with auscultatory percussion and friction of this region, it was possible to obtain a more exact estimate of the size and condition of the thymus than has hitherto been the rule.

Systematic examination of 140 cases shows that the size of the thymus varies according to the age of the child and its nutritive condition, and to certain pathologic conditions.

Normally the area of thymus dulness in children shows a rhomboid form, which extends from the jugular down to the second or third rib, and whose lateral borders are confined to the sternal and parasternal lines. By exact drawings of the clinical findings on a diagram of the anterior thorax they can be correctly compared with the autopsy results.



## A STUDY OF THE PYROGENIC ACTION OF LACTOSE \*

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MINNEAPOLIS

The question whether a food component if introduced into the intermediary metabolism unchanged is capable of developing pyrogenic action has received renewed interest since Finkelstein<sup>1</sup> first published his observations on alimentary intoxication.

Finkelstein designates this fever as alimentary fever because he believes it dependent on the pathologic effect of some food component introduced into a diseased intestinal tract.

Other observers have held similar views, instances of which are the efforts of Krehl and Matthes<sup>2</sup> and Schultes<sup>3</sup> to show this effect for albumoses; also the observations of Weill and Tiberius,<sup>4</sup> who called attention to a definite relationship existing between temperature variations and food given artificially-fed infants.

The so-called buttermilk fever of Tugendreich<sup>5</sup> has been regarded in the light of a sugar fever. Most observers agree that the food component develops pathologic activities only if there is primarily a lesion in the intestinal tract, an alteration in the wall, functional or otherwise, which permits the food component to pass the barrier and enter the intermediary metabolism not properly changed.

This alteration is brought about by inflammatory changes caused according to Bokai<sup>6</sup> by fatty acids, and as Finkelstein<sup>1</sup> and v. Reuss<sup>7</sup> believe and Jacoby<sup>8</sup> and Escherich<sup>9</sup> believed as long ago as 1877 and 1887;

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\*From the Laboratory of Physiology, University of Minnesota. Director, Professor R. O. Beard.

\*Read before the Chicago Pediatric Society.

1. Finkelstein, H.: Ueber alimentäre Intoxikation, *Jahrb. f. Kinderh.*, lxxv, 263.

2. Krehl, L., and Matthes, M.: Ueber die Wirkungen von Albumosen verschiedener Herkunft, *Arch. f. Path. u. Pharmakol.*, xxxvi, 437. Matthes, M.: Ueber die Wirkung einiger subcutan einverleibten albumosen auf den tierischen Organismus, *Deutsch. Arch. f. klin. Med.*, liv, 39.

3. Schultes: Die Beziehungen zwischen Albumosurie und Fieber, *Arch. f. klin. Med.*, lviii, 325, and lx, 55.

4. Weill and Tiberius: La temperature dans les differentes formes d'allaitement chez les nourissons sains, *Rev. mens. d. mal. de l'enf.*, xxi, 168.

5. Tugendreich: Ueber buttermilch Fieber, *Arch. f. Kinderh.*, xlv, 21.

6. Bokai: Experimentelle Beiträge zur Kenntniss der Darmbewegungen, *Arch. f. exper. Path. u. Pharmakol.*, 1888, xxiv, 153.

7. v. Reuss: Die Bedeutung der Kohlehydrate für die Ernährungs-Störungen im Säuglingsalter, *Wien. med. Wchnschr. Nos. 28, 29 and 30*, 1910.

8. Jacoby: Die Pflege u. Ernährung des Kindes, Gerhardt's Handbuch, 1877, p. 409; Milk Sugar in Infant Feeding, *Arch. Pediat.*, 1901, xviii, 801.

9. Escherich: Verhandl. der 5ten Gesellsch. f. Kinderh., Wiesbaden, 1887, 31.

also by lactose or acids developed through the fermentation of the sugar.

That lactose particularly possesses this effect has been abundantly demonstrated both experimentally and clinically, and this has been explained on the basis of experiments by Albertoni<sup>10</sup> and Röhman and Nagano<sup>11</sup> showing that lactose is more slowly absorbed from the intestinal tract than other sugars. Affected by some change or inflammation, the intestinal wall becomes permeable for substances which otherwise it does not permit to pass unchanged.

Meyerhofer and Pribram<sup>12</sup> were indeed able to show increased resorption and heightened permeability of the intestinal wall for such substances as sugar. Similar effects were observed by Cohnheim,<sup>13</sup> who found that toxic substances introduced into the intestinal tract could alter its permeability.

Langstein and Steinitz<sup>14</sup> came to similar conclusions, as did also Ganghofer and Langer.<sup>15</sup>

The fate of lactose when introduced into the human or animal organism has been the subject of much experiment. Most of it directed primarily toward the determination of the tolerance of the organism for lactose and then secondarily toward the factors which influence this tolerance in health and disease.

F. Voit,<sup>16</sup> v. Halasz,<sup>17</sup> Cremer,<sup>18</sup> Blumenthal,<sup>19</sup> Hofmeister<sup>20</sup> and Helmholtz<sup>21</sup> found that the animal organism's tolerance for lactose is

10. Albertoni: *Sal contegno e sull'azione degli zuccheri nell' organismo*, Ann. di chim. et di Farm. Milano, 1891, xiii, 145.

11. Röhmann and Nagano: *Ueber die Resorption und die fermentative Spaltung der Dissacharide im Dünndarm des ausgewachsenen Hundes*, Arch. f. d. ges. Physiol. (Pflüger), xcv, 533.

12. Meyerhofer and Pribram: *Das Verhalten der Darmwand als osmotische Membran bei akuter u. chronischer Enteritis*, Wien. klin. Wchnschr., 1909, xxii, 875.

13. Cohnheim: *Die Resorption im Dünndarm und in der Bauchhöhle*, Ztschr. f. Biol., xxxvii, 443.

14. Langstein and Steinitz: *Laktase und Zuckerausscheidung beim magendarm kranken Säuglinge*, Beitr. z. chem. Phys. u. Path. (Hofmeister), vii, 515.

15. Ganghofer and Langer: *Ueber die Resorption genuiner Eiweisskörper im Magendarmkanal neugeborener Tiere und Säuglinge*, München. med. Wchnschr., 1904, I, 1497.

16. Voit, F.: *Untersuchungen über das Verhalten verschiedener Zuckerarten im menschlichen Organismus nach subcutaner Injection*, Deutsch. Arch. f. klin. Med., lviii, 523.

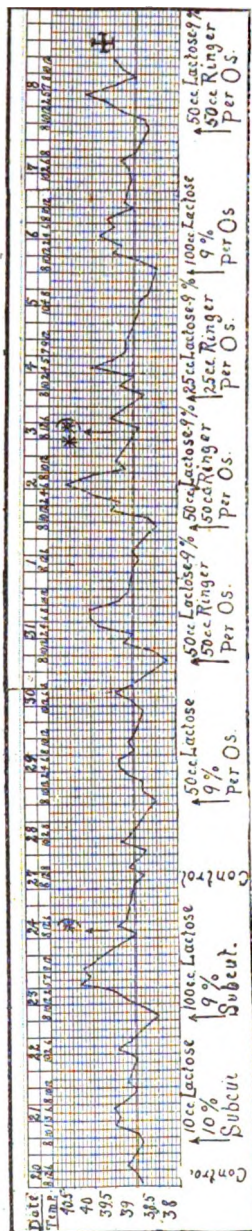
17. v. Halasz: *Die Resorption und das biologische Verhalten der verschiedenen Zuckerarten im Dickdarm*, Deutsch. Arch. f. klin. Med., 1910, xcvi, 433.

18. Cremer, M.: *Zucker und Zelle*, Ztschr. f. Biol., xxxii, 49.

19. Blumenthal: *Zur Lehre von der Assimilationsgrenze der Zuckerarten*, Beitr. z. chem. Phys. u. Path. (Hofmeister), vi, 329.

20. Hofmeister: *Ueber Resorption und Assimilation der Nährstoffe*, Arch. f. exper. Path. u. Pharmakol., xxv, 240.

21. Helmholtz: *Studies on Milk-Sugar*, Arch. Pediat., xxviii, 373.



Charts 1 and 2.—Temperature curves resulting from the giving of lactose and lactose and Ringer's solution to rabbits with intestinal disturbance produced by feeding beta-oxybutyric acid and croton oil. The star in each chart indicates the point at which butyric acid feeding was begun; the double star the point at which croton oil feeding was begun.

lower than for any other sugar. This tolerance sinks particularly low in diseases of the intestinal tract, as was shown by experiments of Grosz,<sup>22</sup> Koplik,<sup>23</sup> Nobécourt<sup>24</sup> and Aschenheim,<sup>25</sup> and more recently by v. Reuss,<sup>26</sup> Leopold<sup>27</sup> and Nothmann.<sup>28</sup>

This led to considerable study of the enzyme lactase, particularly the bearing its presence or absence had on the occurrence of lactosuria. It is present early in life. Miura<sup>29</sup> found it in the intestine of the still-born and Ibrahim<sup>30</sup> and Nothmann<sup>31</sup> in premature infants. Weinland<sup>32</sup> and Orban<sup>33</sup> always found it present in the intestine of the healthy infant but absent in disease. That it is also present in the diseased intestinal tract though in diminished amount was demonstrated by Langstein and Steinitz.<sup>34</sup>

These results and the definite clinical evidence that there seemed close connection between lactose and the production of the pronounced symptoms of alimentary intoxication, principally the fever, led Finkelstein to look on lactose as a substance possessing pyrogenic properties.

The experiments of L. F. Meyer,<sup>34</sup> since confirmed by Friberger,<sup>35</sup>

22. Grosz, J.: Beobachtungen über Glycosurie im Säuglingsalter nebst Versuchen über alimentäre Glycosurie, *Jahrb. f. Kinderh.*, xxxiv, 83.

23. Koplik: Dietetic Glycosuria in Artificially Fed Infants, with Cases, *Arch. Pediat.*, 1892, ix, 781.

24. Nobécourt: De l'élimination par les urines de quelques sucres introduits par la voie digestive ou la voie sous-cutanée chez les enfants, *Rev. mens. d. mal. de l'enf.*, xviii, 161.

25. Aschenheim: Zuckerausscheidung im Säuglingsalter, *Verhandl. d. Gesellsch. f. Kinderh.*, xxvi, 178.

26. v. Reuss: Ueber alimentäre Sacharosurie bei darmkranken Säuglingen, *Wien. klin. Wchnschr.*, 1910, xxiii, No. 4, 123.

27. Leopold: Ueber die Wirkung der verschiedenen Zuckerarten bei ernährungs-gestörten Säuglingen, *Ztschr. f. Kinderh.*, i, 217.

28. Nothmann, H.: Beiträge zur Zuckerausscheidung im Säuglingsalter, ii, 503.

29. Miura: Ist der Dünndarm im Stande Rohrzucker zu invertieren, *Ztschr. f. Biol.*, xxxii, 266.

30. Ibrahim, J.: Zur Verdauungsphysiologie des menschlichen Neugeborenen, *Ztschr. f. physiol. Chem.*, Strassb., 1910, lxiv, 95; Ibrahim, J., and Kaumheimer, L.: Die Doppelzuckerfermente (Laktase, Maltase, Invertin) beim menschlichen Neugeborenen und Embryo, *Ztschr. f. physiol. Chem.*, Strassb., 1910, lxvi, 19.

31. Nothmann, H.: Laktase- und Zuckerausscheidung bei Frühgeborenen Säuglingen, *Monatschr. f. Kinderh.*, viii, 377.

32. Weinland, E.: Beiträge zur Frage nach dem Verhalten des Milchezuckers, *Ztschr. f. Biol.*, xxxviii, 16.

33. Orban, R.: Ueber das Vorkommen der Laktase im Dünndarm und in den Säuglingsfäces, *Prag. med. Wchnschr.*, 1899, No. 33; cited from Maly's *Jahresb. d. Tierchemie*, xxix, 384.

34. Meyer, L. F.: Die Bedeutung der mineral Salze bei den Ernährungsstörungen des Säuglings, *Verhandl. der Gesellsch. f. Kinderh.*, Salzburg, xxvi, 1; Experimentelle Untersuchungen zum alimentären Fieber, *Deutsch. med. Wchnschr.*, 1909, xxxv, 194.

35. Friberger: Untersuchungen über das sogenannte Salzfeber, *München. med. Wchnschr.*, 1909, lxi, 1946.

Schloss,<sup>36</sup> Cobliner<sup>37</sup> and Nothmann,<sup>38</sup> demonstrating conclusively that the Na-halogen group of salts possessed pyrogenic activity, brought out a new factor and caused Finkelstein<sup>39</sup> to regard the pyrogenic action of the sugar as possibly a salt action.

Finkelstein considered that the fever was brought about through some physical action of these substances, essential to which was a preliminary breaking down of the apparatus which maintained the constancy of the tissue fluids. Through this breaking down the salt or the body analogous to it, in this case lactose, entered the circulation in such large amounts that the physiologic state of concentration was altered, and this alteration resulted in fever. There was another possibility. The breaking down of the barrier caused an alteration of vital factors which under normal condition would prevent pyrogenic action of these substances.

From a recent communication it appears that Finkelstein,<sup>40</sup> influenced no doubt by newer investigations, has modified his theory in regard to the pyrogenic effect of lactose in alimentary intoxication to this extent: He believes that under natural conditions (per os) so much is removed by fermentation and resorption that the physical effect (pyrogenic action — analogous to salt action) does not take place. The sugar and the acids developed from it through fermentation largely confine their effect to the production of intestinal lesions (possibly functional) which in turn prevent the proper metabolism of the salts and permit these to develop their physical effect.

Finkelstein's theory that the action of lactose was probably a physical action seemed to be supported by experiments carried on by Schaps<sup>41</sup> in 1907 at the *Kinder-Asyl*.

Schaps observed typical temperature rises after subcutaneous injections of isotonic solutions of NaCl, as well as solutions of dextrose and lactose. The fever reached its fastigium after eight to ten hours and disappeared after twenty-four hours. Only osmotically equal solutions of mono- and dissaccharids seemed to possess pyrogenic action. This fact led Schaps to conclude that the action of sugar was analogous to a salt action, a view which Keller<sup>42</sup> had at one time expressed, and that the pyrogenic effect was brought about in the following manner: Salt or the substance physically analogous to it, in this case lactose, acts pyrogenically when it enters the circulation, either directly, as a substance pos-

36. Schloss, E.: Studien über Salzfeber, *Biochem. Ztschr.*, 1909, xviii, 14.

37. Cobliner, S.: Beiträge zum Kochsalzfeber, *Ztschr. f. Kinderh.*, ii, 439.

38. Nothmann, H.: Zur Frage des Kochsalzfiebers beim Säugling, *Ztsch. f. Kinderh.*, i, 73.

39. Finkelstein: Ueber alimentäre Intoxication, *Jahrb. f. Kinderh.*, lxxviii, 521 and 692.

40. Finkelstein: Personal Communication.

41. Schaps, L.: Salz und Zucker injectionen beim Säugling, *Berl. klin. Wehnschr.*, 1908, xlv, 1309.

42. Keller, A., Czerny, A., and Keller, A.: *Des Kindes Ernährung*, etc., ed. 1, Leipzig, F. Deuticke, i, 326.

sessing pyrogenic action, or by virtue of an alteration in the molecular concentration which its presence in the tissue fluids occasions.

Similar experiments with subcutaneous injections of lactose were carried on in infants and animals by Leopold and v. Reuss.<sup>43</sup> Their results coincided fully with those of Schaps and both arrived at similar conclusions. Leopold has also very recently published some observations on lactose and its connection with temperature rises in alimentary disturbances which seem to coincide fully with Finkelstein's later views as expressed above.

Contrary to these results are some observations which do not coincide with such rises as expressed by Finkelstein or Schaps.

Nobécourt<sup>44</sup> and Keller<sup>45</sup> both injected concentrated solutions of lactose subcutaneously to determine the tolerance for it. Outside of severe local reactions neither author saw untoward toxic effect from these injections and makes no mention of fever. J. v. Kossa<sup>46</sup> reports similar effects. This has raised the doubt in some minds as to whether the temperature recorded by Schaps was not entirely due to local reaction caused by tissue injury at the seat of injection.

Neither F. Voit<sup>47</sup> nor Dastre<sup>48</sup> record any fever reactions with the intravenous administration of lactose. The latter's experiments are particularly interesting since he gave the lactose in physiologic salt solution.

In all the experiments of Gross,<sup>22</sup> Nobécourt,<sup>24</sup> Terrien<sup>47</sup> and Keller,<sup>44</sup> dealing with alimentary glycosuria and lactosuria and the determination of the tolerance the human and animal organism has for the various sugars, no mention is made of pyrogenic effect.

Coblner<sup>49</sup> has recently published the interesting observation that in dyspepsias and alimentary intoxication the sugar content of the blood is not increased.

Rosenthal<sup>49</sup> in an extensive series of experiments on dogs and rabbits was able to show pyrogenic effect for lactose in only a few instances. With salt solution he found even hypothermia and concluded that neither one possessed pyrogenic property or was the principal factor in the production of alimentary fever.

43. Leopold and v. Reuss: Experimentelle Untersuchungen über Milchzucker-ausscheidung nach wiederholten subcutanen Injectionen, *Monatschr. f. Kinderh.*, viii, 1 and 453.

44. Keller, A., Czerny, A., and Keller, A.: Des Kindes Ernährung, etc., i, 320.

45. Kossa, J. v.: Beitrag zur Wirkung der Zuckerarten, *Arch. f. d. ges. Physiol.* (Pflüger), lxxv, 310.

46. Dastre: Observations on Diuresis Produced by Various Sugars, *Compt. rend. Soc. de biol.*, xli, 574.

47. Terrien: De la glycosurie alimentaire chez les nourissons, *Rev. mens. d. mal. de l'enf.*, xviii, 402.

48. Coblner, S.: Blutzucker Untersuchungen bei Säuglingen, *Ztschr. f. Kinderh.*, i, 207.

49. Rosenthal, F.: Zur Frage des alimentären Fiebers, *Jahrb. f. Kinderh.*, lxx, 123.

The experiments of Dastré<sup>46</sup> and F. Voit<sup>46</sup> are the only ones recorded in the literature in which lactose was given intravenously.

At Professor Finkelstein's suggestion I undertook this study which primarily had as its object the observation of the effect of lactose on the body temperature if introduced directly into the blood-stream in varying amounts and under varying conditions. I eventually enlarged on this in order to study the general effect of lactose and compare my results with those of other observers. I selected the rabbit for experimentation on account of the ease with which intravenous infusion and all other manipulations can be carried out on this animal. The technic of the experiment was as follows:

Female rabbits were generally selected and were liberally fed on carrots and other vegetables. The temperature of the rabbit was controlled at regular intervals the day before the experiment. The highest temperature on this day was considered as the control. Any rise above it was considered as a febrile reaction.

The temperatures were taken at regular intervals of from one-half to three hours. The thermometer was introduced about 4 to 5 cm. into the rectum and allowed to remain five minutes. The normal temperature of the rabbit, while somewhat labile, seems to lie between 38.5 and 39.5 C. These figures coincide with extensive observations made on this point by Gibson.<sup>50</sup>

The intravenous and subcutaneous administrations were carried out under absolute aseptic precautions and only sterilized solutions used in all the experiments. The solutions were introduced into a vein of the ear, under the skin of the abdomen, and orally by means of a stomach tube.

In the series of experiments with butyric acid and croton oil feeding, these substances were given orally in watery solution 0.5 per cent. strength and in olive oil 10 minims to 20 c.c., respectively. Eighty experiments were carried out covering in all eight different series.

Five intravenous injections with distilled water in amounts varying from 10 to 75 c.c. were followed three times by febrile reactions, coinciding in this respect with similar experiments of Helmholtz,<sup>51</sup> who believes that this action is due to the destruction of blood cells and the setting free of pyrogenic substances.

Lactose alone was given intravenously twenty-three times in concentration of 5 per cent. up to 50 per cent., and amounts varying from 6 to 50 c.c. There were nineteen positive reactions. The time to the fastigium varied between two and seven and one-half hours. The general rise of temperature for all experiments was 0.36 degree. The highest

50. Gibson: On Proteose Fever, Doctorate Thesis, Yale, 1906.

51. Helmholtz: Pyrogenic Action of Salt Solutions in Rabbits, *Arch. Int. Med.*, vii, 468.

temperature recorded was 1.3 degrees above the control. This animal died five hours after the injection. It had some convulsions. The autopsy was negative.

TABLE 1.—INTRAVENOUS INJECTIONS

Number of Experiments	Conc. in Per Cent.	Quantity Used, c.c.	Time to Fastigium, Hours	Highest Temperature, C.	Rise Above Control, Degrees	Animal*
EXPERIMENTS IN WHICH DISTILLED WATER WAS USED						
1	..	10	...	39.1	0.0	A
6a	..	10	2	40.0	0.6	B
7a	..	20	4	39.7	0.1	B
2	..	50	2	39.8	0.5	A
3	..	75	...	38.6	-0.2	A
Average					0.25	
EXPERIMENTS IN WHICH LACTOSE WAS USED						
1a	5	6	...	38.8	-0.4	B
2a	5	10	7½	40.	0.6	B
3a	5	10	3½	39.8	0.6	B
6	5	20	5	40.	0.5	A
7	5	40	...	39.	-0.2	A
8	9	10	4	39.9	0.2	A
9	9	10	3½	40.0	0.6	A
9a	9	20	6	39.8	0.8	B
10	9	20	4	39.2	0.15	B
10a	9	75	0	39.0	0.0	B
11	10	10	2	40.0	0.4	A
12	10	20	4	39.6	0.1	A
13	10	20	...	39.	-0.1	A
14	10	50	5	40.6	0.8	A
15	10	75	6	40.1	1.1	A
16	10	75	...	39.4	0.1	A
3a	10	100	4	39.9	0.3	B
2a	10	100	5	39.8	0.2	B
11a	20	20	...	39.	0.1	B
12a	20	50	...	39.3	0.1	B
13a	40	60	5	39.2	.00	B
16a	50	50	4	40.6	1.3	B
8a	50	50	5	39.6	0.8	B
Average					0.36	

\* A, unused animal; B, used animal.

In two further series I tried combinations of physiological salt solution and lactose, and Ringer's solution and lactose. The lactose was given in solutions of 9 and 10 per cent., respectively. There was a positive rise of temperature above the control in every instance. The average rise for the series with physiological salt solution and lactose was 0.71 degree and for the series with Ringer's solution 0.9 degree. The time to the fastigium was from two to six hours. The highest rise above the control, 41.6 C., occurred in an unused animal and was the highest temperature observed in any experiment. Whether a used or unused animal was taken for injection seemed to have no effect on the temperature rise.



TABLE 2.—INTRAVENOUS

Number of Experiments	Conc. in Per Cent.	Quantity Used, c.c.	Time to Fastigium, Hours	Highest Temperature, C.	Rise Above Control, Degrees	Animal* . . . .
LACTOSE SOL., PHYSIOL. NaCl SOL. EQUAL PARTS						
25	10 NaCl	20	2	40.8	1.0	A
26	10 NaCl	10	2	40.2	0.8	A
27	10 NaCl	20	2	39.9	0.2	A
29	10 NaCl	10	2	40.8	0.9	A
30	10 NaCl	50	2	40.6	.85	A
Average					0.71	

LACTOSE AND RINGER, EQUAL PARTS

32	10 R	20	4	41.6	2.0	A
31	10 R	10	3½	40.8	1.6	A
27	10 R	20	4	39.9	0.6	B
28	10 R	10	5	39.8	0.4	A
31a	10 R	50	4	40.	0.8	B
30a	10 R	50	4½	39.9	1.0	B
28a	9 R	30	5	40.	0.6	B
26a	9 R	30	4	39.3	0.3	A
Average					0.90	

\* A, unused animal; B, used animal.

TABLE 3.—SUBCUTANEOUS INJECTIONS

Number of Experiments	Conc. in Per Cent.	Quantity Used, c.c.	Time to Fastigium, Hours	Highest Temperature, C.	Rise Above Control, Degrees	Animal* . . . .
LACTOSE USED						
1b	9	20	...	38.8	0.00	B
2b	9	10	4	39.6	0.1	B
3b	9	10	...	39.	-0.2	B
11b	9	20	5	39.9	0.4	B
12b	9	50	3	39.2	-0.1	B
9b	9	50	4	40.0	0.8	B
24a	9	100	7	40.2	1.0	B
22a	9	100	9	40.3	0.9	B
24	9	5	...	39.	-0.1	A
10b	9	5	...	39.2	0.0	B
22	10	10	5	39.5	0.3	A
10c	20	40	9	40.0	0.6	B
Average					0.34	

\* A, unused animal; B, used animal.

Twelve injections subcutaneously given, to my surprise, gave the lowest general average rise of temperature of all the experiments. Only seven animals reacted positively while three failed by 0.1 and 0.2 degree to reach the highest control temperature. The amounts injected varied from 5 to 100 c.c. The concentration of the lactose solution used was 9 per cent., 10 per cent., and one injection of a 20 per cent. solution. Neither the amount of fluid used nor the concentration had any appreciable effect on the temperature. Two animals received successive injections at intervals of a few days. In one the amount injected the first time was 5 c.c. and the concentration 9 per cent. No reaction ensued.

In the second injection the amount was 40 c.c. and the concentration 20 per cent. The reaction following was only 0.6 per cent. higher than the control the day before.

Similarly in the second animal the amounts were 10 and 100 c.c., respectively, followed by reactions of 0.3 and 0.9 degree. None of these animals, with the exception of the one which received the 40 c.c. of a 20 per cent. concentration, showed any pronounced local irritation at the seat of injection. The results are distinctly negative and do not coincide with the findings of either Schaps or Leopold and v. Reuss.

TABLE 4.—ORAL ADMINISTRATION

Number of Experiments	Conc. in Per Cent.	Quantity Used, c.c.	Time to Fastigium, Hours	Highest Temperature, C.	Rise Above Control, Degrees	Animal*
LACTOSE USED						
3c	5	50	...	38.8	0.0	B
4	5	100	5	39.4	0.05	A
5	9	20	...	39.0	-0.1	A
6b	9	20	4	39.3	0.2	B
7b	9	50	...	38.6	-0.4	B
13b	9	100	8	40.0	0.3	B
14b	10	50	...	39.1	0.0	B
15a	20	50	...	38.6	-0.4	B
8b	50	50	6½	40.1	0.8	
					Average	0.15
LACTOSE AND SODIUM CHLORID SOLUTION						
4a	9 NaCl	50	6	39.9	0.3	B
5a	9 NaCl	100	3	39.	0.0	B
17	9 NaCl	30	8	39.6	0.5	A
18	10 NaCl	50	8½	40.0	0.6	A
					Average	0.35
LACTOSE AND RINGER'S SOLUTION						
19	9 R	30	6½	39.5	0.5	A
10d	9 R	50	9	39.3	0.1	B
20	9 R	100	6	40.1	0.9	A
					Average	0.50

\* A, unused animal; B, used animal.

Finally I gave lactose both alone and in combination with physiological salt solution orally. First in a series of healthy rabbits, that is, rabbits free from any apparent alimentary disturbance, and then in a series of rabbits in which more or less pronounced intestinal disturbance had been produced by feeding beta-oxybutyric acid and croton oil, respectively (Charts 1 and 2).

Lactose given alone in amounts varying between 50 and 100 c.c. and in concentration of from 5 to 50 per cent. only once produced an appreciable rise of temperature over the control. This was 0.8 degree, follow-

ing the administration of 50 c.c. of a 50 per cent. solution. In nine experiments only four reactions were shown above the control.

The general average rise for lactose and physiological salt solution and lactose and Ringer was only 0.35 and 0.50 degree, respectively, very little higher than the reactions with lactose alone.

TABLE 5.—ORAL ADMINISTRATION, BETA-OXYBUTYRIC ACID AND CROTON OIL FEEDINGS

Number of Experiments	Conc. in Per Cent.	Quantity Used, c.c.	Time to Fastigium, Hours	Highest Temperature, C.	Rise Above Control, Degrees	Animal*
LACTOSE AND RINGER'S SOLUTION						
10e	9 R	50	4½	40.2	1.0	B
10f	9	50	5	40.	0.6	B
10g	9	50	...	38.9	-0.1	B
10h	9	100	4	40.	0.9	B
10i	9 R	100	9	40.	1.0	B
10j	9 R	100	7½	40.1	1.1	B
23	20 R	50	6	40.	0.8	A
22b	9	50	8	39.8	0.5	B
22c	9 R	100	10	40.	0.6	B
22d	9 R	100	10	40.6	1.6	B
22e	9 R	50	9½	40.	0.5	B
22f	9	100	8	39.8	0.9	B
22g	9 R	100	9	40.1	0.8	B
33	9 R	100	7	41.	1.0	B
33a	9 R	50	...	39.2	-0.3	B
					Average	0.76
LACTOSE AND SODIUM CHLORID SOLUTION						
33b	9 NaCl	100	7½	40.	0.2	B

\* A, unused animal; B, used animal.

The last series in which the rabbits were fed beta-oxybutyric acid and croton oil in order to produce intestinal lesions, proved the most interesting. That this disturbance is quite readily accomplished is evidenced by the diarrhea following the feedings, occurring usually after the fourth day in the oxybutyric acid feeding and somewhat earlier with croton oil. Several autopsies performed on animals just at the onset of the diarrhea showed more or less pronounced inflammatory changes in the intestinal wall. Animals killed at a later stage, in which the feeding had extended over a period of six or seven days, showed still more pronounced inflammatory changes.

The administration of the sugar and combined sugar and salt solutions was begun with the onset of the diarrhea and in several experiments continued at intervals of one and two days. In five of the experiments lactose alone was given in amounts varying from 50 to 100 c.c. and in 9 per cent. concentration. The highest reaction above the control following the giving of 100 c.c. of the solution was 0.9 degree. This same animal in two preceding experiments in which only 50 c.c. of a 9 per

cent. solution were given reacted with a rise of 0.6 degree the first time and failed by 0.1 to reach the control the second time. Subsequently it was twice given 100 c.c. of a combination of lactose 9 per cent. and Ringer's solution, equal parts. The highest reaction in the first experiment was 40, in the second 40.1 C. This was 1 and 1.1 degrees higher than the control. The animal at the time had profuse diarrhea, but showed no pronounced evidence of intoxication.

Lactose 9 per cent. and Ringer's solution combined were given in six other experiments in amounts varying from 50 to 100 c.c. The highest temperature recorded was 41 C. following the administration of 100 c.c. This same animal showed no reaction a few days later with 50 c.c. solution of the same concentration and only a rise of 0.2 degree a day later after the giving of 100 c.c. of equal parts of 9 per cent. lactose and physiologic salt solution.

This animal was given lactose in 9 per cent. concentration alone in one experiment and then in three successive experiments was given equal parts of lactose 9 per cent. and Ringer's solution. The animal at the time had profuse diarrhea and died the day following the last experiment. The temperature rose 1.6 degrees above the control only once in the four experiments. The charts of Animals 10 and 22 are appended.

Reviewing the series as a whole, the reaction was positive in fourteen out of sixteen experiments. Individually also the rises above the control were higher than in any of the other experiments, reaching or exceeding in five instances 1 C. My results are at variance with those of Schaps<sup>41</sup> and Leopold and v. Reuss<sup>42</sup> and coincide in the main with those of Rosenthal.<sup>43</sup>

#### CONCLUSIONS

The results of my experiments warrant the following conclusions:

1. Lactose if given intravenously, subcutaneously or orally, possesses no distinct pyrogenic effect no matter in what concentration or amount it is given.

2. It does possess a definite though not pronounced influence on the temperature if it is given subcutaneously or orally in an animal with a diseased intestinal tract in combination with a medium containing a sodium salt, such as physiologic or Ringer's salt solution.

These results though definite are hardly so to the extent expected when one considers the pronounced effect produced clinically by the administration of lactose in similar conditions, and are far from explaining the pathogenesis of the fever occurring in alimentary intoxication.

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## THE MANAGEMENT OF SQUINT IN CHILDREN

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It is of the greatest importance that those who preside over the physical destinies of children should understand that squint in children is curable. By squint I mean the common form of concomitant convergent strabismus, or "cross-eyes." There are other forms of squint occurring in children which are not curable except through operative measures, but they are comparatively rare.

When I state that the common squint is curable, I mean that it may be cured by non-operative measures, but the pediatricist must understand that the cure depends on the *early* institution of the proper measures and their implicit observance. The responsibility for allowing children to become adults with eyes crossed and loss of function in one eye — an eye otherwise normal — must be shared by three persons, whom I name in the order of their importance.

First, the parents. Many parents have a false pride which leads them into the error that it is more of a stigma to the child to wear glasses than it is to grow up with eyes crossed. (It must be said in justification of them that they are not usually aware that there will also be loss of function in one eye.) Some mothers are too much occupied to possibly give the child such attention as is necessary to carry out the treatment properly. Some parents are too poor to afford the glasses and the necessary repairs. And then there are some too careless or stupid to do their duty by their offspring.

Second, the pediatricist or general practitioner. Nearly every child is taken to a physician for advice when the squint first becomes manifest. Then it is that great stress should be laid on prompt action and the significance of both treatment and neglect should be made clear to the parents. It is not enough to tell the parents that the child should be taken to an oculist. They must be told when and where the oculist can be found and must be made to understand that an optician, by whatever name he may call himself, is not the proper person. Then, to the shame of the medical profession, there are still a few physicians who tell the parents not to be alarmed, that children often "outgrow" squint, and if they do not "it can be straightened when the child is old enough." The family physician is most certain to know of a squint whether he is consulted concerning it or not and it is his business to make inquiries as to what is being done, if anything, for its cure. Many well-meaning

parents do not know the difference between an optician and an oculist and may allow the years during which the child might be cured, to lapse by placing the child in the wrong hands.

Third, the oculist. Once the child reaches the oculist the responsibility rests with him, not only for the management of the squint, but that of the child and its parents as well. If a child is brought very young to the oculist, say at 1 year of age, he should congratulate both himself and the parents, and not tell the parents to bring the child back "when it is old enough to glass." This was formerly a common practice among oculists and is unfortunately still the custom with some.

I believe 100 per cent. of cures are possible, in the class of cases referred to, under the most favorable management, if the children are seen early enough.

It is of importance that every physician should know about the amblyopia; should know that nearly all of these children lose useful vision in one eye, and that the restoration of its function is possible, and a necessary part of the treatment.

Before outlining the individual management of the patient, it is necessary to state the essentials of the etiology. Two factors are responsible for the squint. They may act together or singly.

1. Nearly all such children are far-sighted. Either the cornea is too flat or the scleral axis is too short, so that the rays of light entering the eye are not yet focussed when they reach the retina. This causes the object looked at to be seen indistinctly unless the patient can add to his refraction, by means of the accommodation, sufficient to cause the rays to meet in the macula. This he can usually do and the intuitive desire for clear vision leads him to do so. He accomplishes this by excess stimulus over the third nerve which supplies the muscle of accommodation. Now, since the third nerve also supplies stimulus to the converging group of muscles, and the stimuli for accommodation and convergence are synchronous, an excess also goes to the convergers. When there is no error of refraction neither accommodation nor convergence is required for distance fixation, and for nearer points the amount of stimulus for each corresponds, unit for unit, with the other. But when the patient is far-sighted, stimulus is necessary to the accommodation for distance fixation where no convergence is required, and at nearer points the accommodation stimulus is always in excess of that required for convergence. Since clear vision is the chief function of the eye the accommodation element of the stimulus predominates and too much stimulus is given to the convergence. This would cause the optic axes of the two eyes to cross and a squint to occur in all hyperopes were there not some means by which the patient can compensate for the excess convergence. This he does by sending as much excess stimulus over the sixth nerve to the external rectus muscle as there

is excess convergence, and the eye is drawn tightly back into its suspensory ligament, giving the deep-set eye, characteristic of hyperopia. Or the patient may be able to separate the two stimuli and converge less than he accommodates.

Most hyperopes succeed, in one of these ways, in keeping the optic axes parallel or properly converged, but some fail and squint is the result.

2. The fusion sense presides over binocular single vision, recognizing any failure of the two images to occupy identical points in the two maculas. It is readily understood that no mechanical adjustment could accomplish single binocular vision, when it is known that the size of the image on the retina may not exceed  $1/50$  mm. ( $1/1250$  of an inch.) The fusion sense, acting through the coordination center, is therefore necessary to accomplish this wonderful physiologic feat. Now, the fusion sense, while hereditary, is undeveloped at birth, just as other functions are, and in some children its development is slow or may be arrested. In such a case there is deficient effort made at compensating for the over-stimulus of the convergence in hyperopia and the eyes cross.

If the child happens to be near-sighted there is not sufficient third nerve stimulus and the squint is apt to be divergent. But myopia is more often acquired than congenital, so that the divergent type is not often seen in young children.

#### TREATMENT

The treatment is best considered under the following five heads:

1. Correction of the hyperopia removes the chief cause of the squint and is therefore of prime importance. At what age may a child be glassed? There is no definite answer to this question, but instances are very rare in which the eyes become permanently crossed in a child too young to wear glasses, if it can have proper supervision. Rarely is the patient seen before the age of 1 year, because the visual function is not sufficiently established before this age to call the accommodation into use for sharp vision. Young children take to glasses as they do to shoes or any other wearing apparel and give little trouble after the first week. It is my custom to glass them when first seen unless I am convinced that the glasses will not be worn, either from pride or lack of attention on the part of the parents. A former objection to early glassing was the difficulty in knowing what to order while the child was too young to read, but retinoscopy has eliminated this difficulty.

2. Atropin may be used to suppress the accommodation and render third nerve stimulus of no avail in helping the visual acuity, and the patient will soon cease the effort, incidentally ceasing to overstimulate convergence. This method, once much employed, should only be used when glasses are out of the question, and until such a time as the child may be glassed. It must be used in both eyes two or three times daily.

3. Cure of the amblyopia is essential if single binocular vision is ever to be established. Amblyopia is a form of partial blindness, of cerebral location. It comes about as the result of suppression of the image stimulus from one eye, in an effort to be free from diplopia. All these little patients doubtless see double at first, but are too young to explain the diplopia or even to know that it is unusual. As they learn that one object is false, and it perhaps leads them to make mistakes in taking hold of objects, they begin to ignore the dimmer one — and one is always dim because focussed on the peripheral retina where acuity is low. This suppression soon becomes permanent and some effort is required to give the child diplopia even with a small light and colored glass.

The squinting eye is now unable to see well even with its fellow covered, and is said to be amblyopic. The degree of amblyopia depends somewhat on the duration of the squint. Its cure depends on the forced use of the squinting eye, by occlusion of the good eye. Occlusion may be accomplished by a bandage worn permanently, for six weeks to two years, but since this is objectionable a better plan is to have a highly concave, neutral, frosted lens fitted closely over the good eye, while the proper correction is worn on the amblyopic eye. The obscured lens must rest against the side of the nose, fit closely around the rim of the orbit, and be turned back somewhat at the temporal end. This leaves room for the lashes without allowing the child to see around it. It must be worn constantly. This is not difficult to attain in very young children, say under the age of 5 years, but requires close watching for a month or so in older ones. The child should be kept in the room with its mother, if necessary tied to her apron-strings, until thoroughly accustomed to the use of the amblyopic eye. It is sometimes necessary to use atropin in the covered eye as an aid to prevent peeping around the glass.

I use this method as a routine and find it always successful in patients seen before they are too old. It is difficult of application after the seventh or eighth year. The cover should not be removed until the visual acuity is 20/30 or better. Both eyes are then glassed with the proper correction.

4. The fusion sense must be reestablished. If it were not originally at fault it becomes eliminated, and binocular single vision is impossible without it. In many cases it requires no treatment, resuming its function when the images can be fused. When the squint is of long standing, fusion may not be resumed without encouragement. For this purpose there are several instruments, all based on the principle of stereoscopic vision. Companion pictures are used and are either moved until they fuse or prism aid is given until fusion takes place while the child watches the pictures. The child is thus encouraged to see the same object with both eyes at the same time, without diplopia; i. e., single binocular vision is reestablished.



5. Operative measures are to be used only as a last resort and will very rarely be necessary if the child is properly managed from the incipency of the squint. In patients not seen early or not properly managed, it becomes necessary to "straighten" the eyes in a mechanical way. This is done by shortening the external rectus, one or both, and tenotomizing the internus. The former is to be preferred to the latter and in any case full correction is to be avoided, as the future tendency is outward and a divergent squint may result in adult life. The operation should not "straighten" but aid other measures to do so. No patient should be operated on until the correction has been worn at least one or two years. The technic of the operative measures is not of interest here.

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# PROGRESS IN PEDIATRICS

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## RECENT ADVANCES IN OUR KNOWLEDGE OF RACHITIS

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### ETIOLOGY

Schmorl<sup>1</sup> gives a very extended review of the subject and I shall use his work freely without further reference to it. The following hypotheses have been advanced and are supported by more or less pathologic-anatomic data:

Artificial rachitis in animals: Most of the authors who have undertaken these experiments believe that rachitis is a disturbance of the calcium metabolism, and that it results either from giving too little calcium in the food, or that the normal calcium in the food is not absorbed in sufficient amounts, or finally, that it is absorbed and the bones are not able to assimilate it in a normal manner. The experiments have led to varying results. In most instances feeding a calcium-poor food, or an acid food, or a combination of the two, has resulted in a disease of the bone which was, in gross appearance, very similar to rachitis. Miwa and Stoeltzner<sup>2</sup> found that there were certain differences between this artificial disease of the bone and true rachitis. There was slight disturbance in the endochondral ossification and a very considerable "osteoporose" and Stoeltzner therefore called this artificial disease pseudo-rachitic osteoporosis.

Götting<sup>3</sup> and Schmorl confirmed these results. Clinically the rosary and enlarged epiphyses come in those cases in which there is a deficit of calcium in the bone. Such bone is more easily broken. It is a generally accepted fact that pseudorachitic osteoporosis comes as a result of a calcium-poor food; that it is the physiologic reaction of an organism with healthy bones; and that the bone substance is qualitatively normal but

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1. Schmorl: Die pathologische Anatomie der rachitischen Knochenkrankung mit besonderer Berücksichtigung ihrer Histologie und Pathogenese. *Ergebn. d. inn. Med. u. Kinderh.*, 1909, iv, 403.

2. Miwa and Stoeltzner: Ueber die bei jungen Hunden durch kalkarme Fütterung entstehende Knochenkrankung, *Beitr. z. path. Anat. u. allg. Path.*, 1898, xxiv, 578.

3. Götting: Ueber die bei jungen Tieren durch kalkarme Ernährung und Oxalsäurefütterung entstehenden Knochenveränderungen. *Virchow's Arch. f. path. Anat.*, 1909, cxvii, 1.

has quantitatively less calcium than the corresponding normal bone. This phase of the subject will be treated in more detail later.

An acid food causes the same microscopic picture as a food containing a diminished amount of calcium and must come into the same class as pseudorachitic osteoporosis.

Recently an attempt has been made to prove that some of the diseases of metabolism are due to a disturbance of the function of certain glands having an internal secretion. These are, respectively, the thyroid, parathyroid, thymus and adrenal glands. These attempts have not been successful.

Finally, rachitis has been considered an infectious disease. Schmorl has been unable to isolate any organism to which he could attribute rachitis, except in the case of two rats twenty-four hours old with a disease of the bone which was morphologically similar to a moderately severe rachitis. These observations corresponded with those of Morpurgo,<sup>4</sup> who found a diplococcus in the bones of young rats which were clinically rachitic. J. Koch<sup>5</sup> believes that negative findings are due to poor staining methods and the difficulty of demonstrating bacteria in bones. He was able to demonstrate bacteria both in culture and section in the epiphyses of ribs of children with rachitis who had died in the course of measles, diphtheria, pertussis, scarlet fever, gastro-enteritis, etc. The kind of bacteria found in his cases were often different, and most prominent among them were streptococci, bacteria coli, and staphylococci. In the majority of these cases the heart blood was sterile and the bacteria which were found in the epiphyses were not part of a general infection. He concludes with Kassowitz that rachitis is principally a vascular change of the epiphyses and adds that this change is due to bacterial infection of the part.

#### PATHOLOGY

##### *The Calcification of Bone in Rachitis*

Lehnerdt<sup>6</sup> summarizes the literature on this phase of the subject from seventy odd papers, the references for which will not be given in this review but may be found in the original.

According to Pommer, all newly formed bone first deposits osteoid material which later becomes calcified. This calcification goes on so

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4. Morpurgo: Ueber eine infectiöse Form der Knochenbrüchigkeit bei weissen Ratten. Verhandl. d. Deutsch. path. Gesellsch., 1900, iii, 40; Beobachtungen an Serienschnitten von osteomalacischen und rachitischen Knochen. Verhandl. d. Deutsch. path. Gesellsch., 1909, xiii, 51.

5. Koch, J.: Untersuchungen über die Lokalisation der Bakterien, das Verhalten des Knochenmarkes und die Veränderungen der Knochen, insbesondere der Epiphysen, bei Infektionskrankheiten mit Bemerkungen zur Theorie der Rachitis. Ztschr. f. Hyg. u. Infektionskr., 1911, lxix, 436.

6. Lehnerdt: Warum bleibt das rachitische Knochengewebe unverkalkt? Ergeb. d. inn. Med. u. Kinderh., 1910, vi, 120.

quickly in health that the osteoid layer remains thin. In rachitis the characteristic picture is one with a broad osteoid layer which is the result of some interference with the deposit of lime salts.

Other writers believe that the abnormal amount of osteoid tissue in rachitis is due to the fact that calcium has been robbed from the bone which was once calcified, and others that all bone substance formed during the active or florid stage of rachitis was uncalcified.

A calcium deficit in the bones in rachitis may be attributed theoretically to the following causes:

I. A primary deficit of calcium in the food.

II. A secondary deficit of calcium, there being sufficient calcium in the food.

(a) It is either not absorbed in sufficient quantities for the needs of the growing bone, or

(b) It is absorbed in sufficient quantity but is excreted again in abnormal amounts; and

(1) Either considerable calcium is lost as a result of an abnormal digestion, or

(2) A sufficient quantity is absorbed into the organism, but for some reason cannot be used in the bone and therefore is excreted again.

#### I. PRIMARY CALCIUM DEFICIT

It has long been known that rachitic bones are poor in calcium and on the basis of this knowledge an attempt was made to produce artificial rachitis in animals by feeding them food low in calcium. These experiments caused clinical changes similar to those seen in rachitis and the question came up as to whether true rachitis was produced or not. Chemical analyses of these bones showed that they had a low ash and calcium content. Stoeltzner and Miwa's experiments showed that these changes were not outside of physiologic limits, and these writers concluded that they had to deal with a pseudorachitis giving it the name pseudorachitic osteoporosis. These bones, as mentioned above, show a low ash and calcium content, but they do not lose relatively as much magnesium as do the bones of true rachitis. In the former the loss of phosphoric acid goes hand in hand with the loss of calcium, while in the latter there is relatively less phosphorus lost than calcium.

The rosary and enlargement of the epiphyses comes in all cases in which there is a diminution in the deposit of calcium. Such bones are easily broken. Finally, in pseudorachitic osteoporosis the abnormally broad zone of growth cannot be demonstrated under the microscope and is always present in true rachitis. The two diseases are, therefore, best differentiated by the pathologist. On the basis of these facts Lehnerdt agrees with Stoeltzner and Miwa that pseudorachitic osteoporosis is a

result of a food containing a low amount of calcium, is the physiologic reaction of an organism with healthy bones to a calcium-poor food and that the bone substance is qualitatively normal and quantitatively diminished in amount. A deficit of calcium in the food, therefore, cannot cause true rachitis.

Aron<sup>7</sup> concludes that the normal infant takes only as much calcium from human milk as it requires for growth. Some of the cases in which rachitis develops on human milk are due to too small a percentage of calcium in the milk.

Bahr<sup>8</sup> and Edelstein<sup>9</sup> found the average CaO in human milk to be 0.0426 per cent., while Schabad<sup>9</sup> found that the calcium content of human milk is greater at the beginning of nursing than at the end, and that there is a progressive diminution in the percentage of calcium during the course of lactation, falling off from 0.045 per cent. to 0.031 per cent. The decrease is constant and regular in some women and in others irregular and with great variations. The average percentage of calcium in human milk on which healthy babies were fed is 0.044 per cent. and rachitic babies 0.039 per cent. Rachitis is possible with a large percentage of calcium in the milk, even with 0.055 to 0.088 per cent. The milks on which children develop rachitis contain larger amounts of the organic constituents, for example, fat, than do the milks of healthy babies. The caloric value of the rachitogenic milk is therefore higher. For every 100 milk calories in rachitis there were 63 mg. of calcium and in health 76.5 mg. It is obvious, therefore, that the rachitic baby must either take the required amount of food calories containing too little calcium or to obtain the necessary quota of calcium it must take too much food. It is, according to Schabad, impossible to increase the amount of calcium in human milk. He believes that the clinical manifestations due to a calcium deficit in the food are not true rachitis but are pseudo-rachitic osteoporosis.

## II. SECONDARY CALCIUM DEFICIT

Sufficient proof has not been obtained from complete metabolism experiments to warrant the conclusion that a decrease in the retention of calcium is responsible for its decreased absorption. Either the gastrointestinal canal must be in such a condition that there is an increased excretion of calcium or the newly formed bone is in such condition that, during the active stages of rachitis, the calcium which has already been

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7. Aron: Kalkbedarf und Kalkaufnahme beim Säugling und die Bedeutung des Kalkes für die Aetiologie der Rachitis. *Biochem. Ztschr.*, 1908, xii, 28.

8. Bahr<sup>8</sup> and Edelstein: Das Kalkangebot in der Frauenmilch. *Jahrb. f. Kinderh.*, 1910, lxxii, Suppl., p. 16.

9. Schabad: Der Kalkgehalt der Frauenmilch. Zur Frage der ungenügenden Kalkzufuhr als Ursache der Rachitis. *Jahrb. f. Kinderh.*, 1911, lxxiv, 511.

absorbed into the body<sup>1</sup> cannot be deposited in the normal manner and is therefore reexcreted into the intestine.

Birk<sup>10</sup> and Rothberg found that there was a negative calcium balance (i. e., more calcium was excreted from the body than was ingested in the food) in those cases in which there were large amounts of fat in the food. In their whole milk experiments the ash balance was always negative, this being more marked in young children, and both these writers concluded that milk-fat had an unfavorable influence on the retention of ash, more especially calcium and magnesium. They believed, furthermore, that there was first an excess of fatty acids in the intestine and that these fatty acids withdrew the salts (among them calcium) from the body to form soaps. The calcium retention increased as the soap formation decreased. Birk concluded that rachitis was due to a primary disturbance of digestion. Lehnerdt considers that this conclusion is not based on sufficient proof, especially because the fatty acids can combine with only relatively small amounts of the alkaline salts. Bahrdr<sup>11</sup> considers that there were more bases excreted by the rachitic children reported by Birk, than could be combined with the soaps present. Freund<sup>12</sup> found that with an increase of fat and the formation of soap stools there was no diminution in the calcium balance.

Birk<sup>13</sup> performed a series of experiments on two healthy and two rachitic children to see if cod-liver oil had an unfavorable action on the digestion of fat and caused demineralization of the body. The action of the cod-liver oil and phosphorus caused a doubtful negative mineral balance to improve in the two rachitic children and had no effect on the healthy children because they retained only as much mineral salts as they needed in growth. The absolute amount of soaps in the stools of the rachitic children was considerably larger than that in the stools of the healthy children, while the percentage of soap in the stools of the rachitic children was reduced. Freund<sup>14</sup> commented on the fact that the absolute amount of soap in the stools of the healthy children was the same before and after the administration of phosphorus and cod-liver

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10. Birk: Ueber den Magnesiumsatz des Säuglings. *Jahrb. f. Kinderh.*, 1907, lxvi, 300; Rothberg: Ueber den Einfluss der organischen Nahrungskomponenten auf den Kalkumsatz künstlich genährter Säuglinge. *Jahrb. f. Kinderh.*, 1907, lxvi, 69.

11. Bahrdr: Untersuchungen über das Symptom der Seifenbildung und die Ausscheidung der Basen im Darm des Säuglings. *Jahrb. f. Kinderh.*, 1910, lxxi, 249.

12. Freund: Zur Wirkung der Fettdarreichung auf dem Säuglingstoffwechsel. *Jahrb. f. Kinderh.*, 1905, lxi, 36.

13. Birk: Untersuchungen über den Einfluss des Phosphorlebertrans auf den Mineralstoffwechsel gesunder und rachitischer Säuglinge. *Monatschr. f. Kinderh.*, 1908, vii, 450.

14. Freund: Physiologie und Pathologie des Fettstoffwechsels im Kindesalter. *Ergebn. d. inn. Med. u. Kinderh.*, 1909, iii, 139.

oil and that in the rachitic children there was a lower percentage of soap and a larger amount of neutral fat and fatty acids when using phosphorus and cod-liver oil. If the soaps were responsible for the loss of calcium in rachitis the condition would be similar to that produced in animals and there would result not rachitis but pseudorachitic osteoporosis.

Lehnerdt apparently considers the following hypothesis of Stoeltzner most plausible — that the newly formed bone remains uncalcified because it is not in condition to impregnate itself with the calcium which is brought to it in the body fluids. When the calcium is rejected by the bone it must be excreted and returned to the intestine, where it combines with the fatty acids to form soaps. If this is true, calcium is the cause of the excessive formation of soaps instead of being a result of an abnormal fat digestion.

The acid theory of the pathogenesis of rachitis is without foundation because animals fed on acids do not develop rachitis and there is no diminution in the alkalinity of the blood.

Stoeltzner's<sup>15</sup> theory that the bone in rachitis is unable to deposit calcium in the normal manner is developed as follows: There are three stages in the development of bone: (1) the osteoid, in which the bone does not possess the power of depositing salts; (2) the potential, in which it obtains the power, and (3) the actual, in which calcium is deposited. If there is too little calcium in the food the stages progress in a normal manner except that the advance from the potential to the actual stage of deposited calcium should not take place because of the lack of calcium, and one should find abnormal amounts of osteoid tissue. This, however, is not the case. The old bone, which has already calcified, gives up its calcium to the new bone and the new bone continues to develop in the normal manner, passing from the potential to the actual stage. Thus the newly formed bone is constructed at the expense of the old bone because there is not enough calcium at hand to supply all the demands of the growing skeleton. The abnormally broad zone of osteoid tissue of true rachitis is not seen in experimental rachitis (pseudorachitic osteoporosis) because there is merely a deficit of calcium in the food, and not a condition which makes it impossible to deposit calcium.

Lehnerdt<sup>16</sup> experimented with animals and found by substituting strontium for calcium in the food, that bone changes only came when there was a deficit of calcium. The severity of strontium pseudorachitis

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15. Stöltzner: Die zweifache Bedeutung des Calciums für das Knochenwachstum. Arch. f. d. ges. Physiol. (Pfüger), 1908, cxxii, 599.

16. Lehnerdt: Zur Frage der Substitution des Calciums im Knochensystem durch Strontium. I. Der Einfluss des Strontiums auf die intrauterine Entwicklung des Knochensystems. Beitr. z. path. Anat. u. z. allg. Path., 1909, xlii, 468; II. Strontiumfütterung an säugende Tiere. Beitr. z. path. Anat. u. z. allg. Path., 1909, xlvii, 215; Phosphorsklerose und Strontiumsklerose, Jahrb. f. Kinderh., 1910, lxxii, 395, 610.

depends on the amount of the deficit. This condition is rapidly cured when calcium is again given in the food. Lehnerdt concludes, as a result of his own observations, that true rachitis is in all probability a disturbance of the intermediary metabolism and he considers that "domestication" plays an important rôle in the subject. Rachitis is not a disease of the free, wild animal, but is often found in animals confined in zoological gardens. Similarly the children of a pastoral race are apt to develop it when confined to a city.

v. Hausemann<sup>17</sup> considered that it resulted from too little air and activity. For example, those children born in the fall who are necessarily housed all winter in bad quarters and with poor ventilation had rachitis more frequently than children born in the spring and living under the same circumstances. Schmorl<sup>1</sup> found that in a great majority the disease commenced between the months of November and March. They tend to cure spontaneously during the summer months and to relapse in the fall. Ebbell's<sup>18</sup> attention was attracted to the question of why rachitis is a relatively rare disease in the tropics. A study of its geographical distribution shows that it increases in frequency the greater the distance from the equator, irrespective of race. He concludes that rachitis is the result of lack of light. This assumption was apparently confirmed by some experiments on animals and plants which were deprived of light and in which deformities developed. He thinks that the ultraviolet ray is particularly important and points out that this ray is partially arrested by window glass. Therefore children kept in the house are deprived of the ultraviolet ray in particular. Sittler<sup>19</sup> believes that it is a true disturbance of digestion which is caused in part by unhygienic surroundings, more especially during the winter months. Czerny<sup>20</sup> defines rachitis as a congenital constitutional anomaly whose most prominent symptom is the change in the bones and cartilages. There is evidently a general disturbance of nutrition affecting the bones and inducing symptoms on the part of the nervous system. Hutinel<sup>21</sup> regards a quantitative modification of the bone-marrow as the essential feature of rachitis. He thinks that the qualitative changes are similar to those encountered in ordinary infections; but the remarkable proliferation of the bone-marrow seems to be specific for rachitis. Marfan<sup>22</sup> says that one must admit that all

17. v. Hausemann: Ueber Rachitis als Volkskrankheit. Berl. klin. Wchnschr., 1906, xliii, 249.

18. Ebbell: Norsk Mag. f. Lægevidensk., 1909, lxix; abstr. in Jour. A. M. A., 1908, 1, 1390.

19. Sittler: Neuere Ansichten über die Aetiologie der Rachitis. Fortschr. d. Med., 1909, xxvii, 817.

20. Czerny: Die erste Vorlesung in Strassburg, 9 Mai, 1910; Monatschr. f. Kinderh., 1910, ix, 131.

21. Hutinel: LeRachitisme. Arch. de méd. des enf., 1910, xiii, 81.

22. Marfan: Le Rachitisme et sa pathogenie bailliere et fils, Paris, 1911.



rachitis carry a focus of infection or chronic intoxication. Rachitis does not act like a special single disease but a syndrome in which bony deformity is the most prominent symptom.

The work of Schabad and his pupils on rachitis has been prominent in medical literature and has added much to our knowledge of normal and diseased bone. He<sup>23</sup> found that the dried bones of the newly born infant contained 60 to 65 per cent. of ash and 40 to 45 per cent. of organic material. The amount of ash in the bone varies from birth onward; at first the ash increases and at the second year decreases to 59 to 55 per cent. and during this time there is a corresponding increase in the organic material. The ash begins to increase at the end of the second year up to the adult 68 per cent. of the dried bone substance. The percentage of water in rachitic bone is higher and the percentage of dry substance is lower than in healthy bone. The relation of ash to organic matter is 20:80 in rachitic bone and 60:40 in healthy bone. Krasnogorski<sup>24</sup> also found a high water content in rachitic bones with a mineral content of one-half the normal. The calcium and magnesium were especially reduced. These facts left no doubt in the author's mind that the large amount of water in rachitic bones stands in causal relation to the poverty of calcium ions. The disturbance of the intracellular calcium metabolism must change the water content of the organism and have a powerful influence over the entrance of water into the organism. Under this influence the hyaline substance of the bone absorbs water and there results the clinical enlargement of the epiphyses of rachitis. Gassmann<sup>25</sup> concludes as a result of his analyses of healthy and rachitic bones that the complex salt  $(Ca_2(PO_4)_2)3CaCO_3$  is the same in both instances. Potassium, sodium and chlorin are the same in both but magnesium is increased from 0.50 per cent. in normal bone to 0.53 to 0.74 per cent. in rachitic bones. He concludes, therefore, that magnesium plays an important part in the pathology of the disease.

Schabad<sup>26</sup> reports further that the weight of the skeleton during the first year of life is 16 per cent. of the body weight. The calcium content of the skeleton is 1.25 per cent. of the body weight and 7.7 per cent. of the skeletal weight. The greatest deposit of calcium takes place during the period of greatest growth, i. e., in a breast-fed baby between the second

23. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis. Der Mineralgehalt gesunder und rachitischer Knochen. Arch. f. Kinderh., 1909, lli, 47.

24. Krasnogorski: Ueber die Wirkung der Ca-Ionen auf das Wasserabsorptionsvermögen der Knorpelgewebes und ihre Bedeutung in der Pathogenese des rachitischen Prozesses. Jahrb. f. Kinderh., 1909, lxx, 643.

25. Gassmann: Chemische Untersuchungen von gesunden und rachitischen Knochen. Hoppe-Seyler's Ztschr. f. physiol. Chem., 1910, lxx, 161.

26. Schabad: Zur Bedeutung der Kalkes in der Pathologie der Rachitis. II. Der physiologische Kalkbedarf und Rachitis infolge von unbefriedigtem Kalkbedarf. Arch. f. Kinderh., 1910, lli, 68.

and fourth months, and in a bottle-fed baby between the second and sixth months. The calcium retention of a baby taking human milk may be as high as 70 per cent. of the intake and one taking cows' milk 30 per cent. Although the calcium content of cows' milk is four times greater than that of human milk, the calcium needs during the period of greatest growth can only be furnished by two-thirds milk or richer, because the assimilation of cows' milk is two and one-half times poorer than human milk. A baby may take human milk containing deficient calcium for three months' time without any symptoms of rachitis, and therefore the connection between a low percentage of calcium in the food and rachitis is not established. Rachitis, on the other hand, may develop in a baby taking human milk containing the normal or a diminished amount of calcium. He agrees with Stoeltzner that experimental rachitis caused by feeding animals a calcium-poor food is clinically, anatomically and chemically indistinguishable from spontaneous rachitis, but that histologically it is characterized as a pseudorachitic osteoporosis. Furthermore, it is probable that in man there is a condition other than rachitis in which a deficient amount of calcium in the food causes a pseudorachitis which cannot be differentiated clinically from rachitis, but which has the characteristics of pseudorachitis.

In acute rachitis<sup>27</sup> and during the early or florid stage of the disease the calcium balance is either diminished or negative, and as the disease progresses and becomes well developed the calcium balance is either below normal or within normal limits. When convalescence commences there is increased retention of calcium which shows itself earlier than does clinical improvement. During this latter period two to three times more calcium is retained than is normal and when the cure is complete the calcium retention again becomes normal.

The increased excretion of calcium in progressive or florid rachitis goes on exclusively through the intestines and at the same time there is less calcium than usual excreted through the urine. Dibbelt<sup>28</sup> obtained the same results and believes that this is evidence against the theories of increased resorption of calcium from the bones or of inability of the rachitic osteoid tissue to take up calcium, because, according to him, they are not compatible with the decreased absorption of calcium in the urine. In either of these condition the urinary calcium should be increased. Schabad interprets these findings as evidence against the acid theory of rachitis.

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27. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis: III. Der Kalkstoffwechsel bei Experimenteller. *Arch. f. Kinderh.*, 1910, liii, 380.

28. Dibbelt: Weitere Beiträge zur Pathogenese der Rachitis. *Verhandl. der deutsch. path. Gesellsch.*, 1910, xiv, 294.

The relation between calcium and phosphorus was then studied by Schabad<sup>29</sup> and he found that there was an increased excretion of phosphorus as well as calcium in the acute stage of rachitis. There was relatively so much phosphorus excreted that it could not all have come from the bone and presumably was lost from the phosphorus-rich nervous system. The relation between the phosphorus in the urine and feces in nurslings is 80:20 in health and 65:35 in rachitis; and in the bottle-fed baby 60:40 in health and 40-44:60-56 in rachitis. During convalescence from rachitis the total excretion of phosphorus is lower than normal and the relation between the phosphorus in the urine and the feces returns to the normal figures. The following connection has been established between the calcium and phosphorus excretion: An increased excretion of calcium causes a greater retention of phosphorus, and vice versa. The great loss of phosphorus is important in the disease and may explain the nervous symptoms. Birk and Orgler<sup>30</sup> found that a disturbance of the calcium metabolism may be present quite a while before the clinical appearance of rachitis. Orgler<sup>31</sup> criticizes Schabad's deductions and does not consider them free from error. In one instance he was able to increase the calcium retention by changing the quality of the food, and in another instance an increase in the amount of calcium in the food did not influence the calcium retention at all. Orgler believes that there are two important conditions which regulate the assimilation of calcium: (1) the power of the body to assimilate it, which depends on the intermediary metabolism concerning which we know nothing; and (2) the composition of the food. Aschenheim and Kaumheimer<sup>32</sup> examined the muscles of eight children with rachitis and three without rachitis and found that in all cases of rachitis there was a diminution in the amount of calcium which apparently corresponded with the severity of the disease. Bing<sup>33</sup> found excessive thinning of the muscle fibers with loss of striation accompanied by an increase of the muscle-cell nuclei without interstitial infiltration. He found these changes less marked in milder forms of rachitis and never found the same condition in the control muscles examined.

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29. Schabad: Zur Bedeutung des Kalkes in der Pathologie der Rachitis: IV. Der Phosphorstoffwechsel bei Rachitis. Arch. f. Kinderh., 1910, liv, 83.

30. Birk and Orgler: Der Kalkstoffwechsel bei Rachitis. Monatschr. f. Kinderh., 1910, ix, 544.

31. Orgler: Ueber den Kalkstoffwechsel bei Rachitis. Monatschr. f. Kinderh., 1911, x, 373.

32. Aschenheim and Kaumheimer: Ueber den Aschegehalt der Muskulatur bei Rachitischen. Monatschr. f. Kinderh., 1911, x, 435.

33. Bing: Histopathologische und Elektrodiagnostische Untersuchungen bei rachitischen Kindern mit pseudoparetischen und atonischen Muskelstörungen. Med. Gesellsch., Basel, Dec. 6, 1906; Reported in Cor.-Bl. f. Schweiz. Aerzte, 1907, xxxvii, 119.

Findlay<sup>34</sup> examined the blood in rachitis and summarized his findings as follows: In active and uncomplicated rickets anemia is not the rule but is to be regarded as exceptional, and when it occurs is due to adventitious causes. On the contrary, the amount of hemoglobin and the number of red cells in rachitic children in the series examined are notably in excess of the normal average. The red blood corpuscles, as a rule, vary more in size than in normal individuals of similar ages, but otherwise there is no abnormality. The nucleated red cells, polychromatophils and myelocytes are of the rarest occurrence. In rickety subjects there is little characteristic change as far as the leukocytes are concerned. They may be normal, slightly increased, or even diminished in number. The mononuclears more frequently than the polynuclears show an absolute increase in the number per cubic millimeter.

#### TREATMENT

Kassowitz<sup>35</sup> first recommended phosphorus in the treatment of rachitis. His original prescription, known as phosphorlebertan (phosphori 0.01, ol. jecor aselli, ad 250), still holds first place in Germany in the treatment of rachitis. Kissel<sup>36</sup> found in his experiments on animals that phosphorus had absolutely no effect on the skeletal system, and concluded that there was no ground for its use. Despite this report phosphorus continues to be used and many experiments have been performed to prove its efficiency.

Birk<sup>37</sup> and Schabad<sup>38</sup> both concluded that phosphorus in therapeutic doses does not affect the calcium metabolism in healthy children. Such children take only as much phosphorus as they need for growth regardless of the amount in the food. In rachitis cod-liver oil increases the retention of phosphorus and calcium and this action is intensified by the addition of phosphorus to the oil.<sup>39</sup> The increased retention of calcium starts three to five days after giving phosphorus and gradually diminishes until at the end of two months it is again normal. This depends on the increased absorption and decreased excretion through the urine and feces. The question now comes up as to whether oils as such in combination with

34. Findlay: The Blood in Rickets. *Lancet*, London, 1909, i, 1164.

35. Kassowitz: Die Phosphorbehandlung der Rachitis. *Ztschr. f. klin. Med.*, 1883-4, vii, 36.

36. Kissel: Ueber die pathologisch-anatomischen Veränderungen in den Knochen wachsender Tiere unter dem Einfluss minimaler Phosphordosen. *Virchow's Arch. f. path. Anat.*, 1896, cxliv, 94.

37. Birk: Untersuchungen über den Einfluss des Phosphorlebertrans, etc. *Monatschr. f. Kinderh.*, 1908-09, vii, 450.

38. Schabad: Der Phosphor in der Therapie der Rachitis. Der Einfluss des Phosphors auf den Kalkstoffwechsel bei rachitischen und gesunden Kindern. *Ztschr. f. klin. Med.*, 1909, lxxvii, 454.

39. Schabad: Die Behandlung der Rachitis mit Lebertran, Phosphor und Kalk. *Ztschr. f. klin. Med.*, 1909, lxxviii, 94.

phosphorus have a therapeutic action on rachitis. Schabad<sup>40</sup> investigated the action of phosphorus, cod-liver oil and "sesamol" on the metabolism of calcium, phosphorus, fat and nitrogen and found that "sesamol" and phosphorus did not help rachitis, while cod-liver oil plus phosphorus increased the retention of phosphorus and calcium and the absorption of fat and nitrogen. Schabad and Sorochowitsch<sup>41</sup> used lipanin, i. e., olive a substitute for cod-liver oil, which was supposed to be easily absorbed because it contained free fatty acids. They concluded from their metabolism experiments that lipanin and olive oil increase the absorption of nitrogen and fat but that lipanin has no advantage over olive oil. Lipanin does not increase the retention of calcium in rachitis and is therefore not as good as cod-liver oil in the treatment of rachitis. They say in their most recent article<sup>42</sup> that sometimes phosphorus and cod-liver oil does not have a favorable action on the retention of calcium in rachitis, especially if the disease is not approaching a convalescence. At other times they have a favorable action on the calcium retention. They experimented with various other salts combined with cod-liver oil and found that a calcium acetate cod-liver oil had the most favorable action on rachitis because it contained much more calcium.

Most recently Caroline Towles<sup>44</sup> did a series of metabolism experiments in von Pirquet's clinic in Breslau and was unable to demonstrate that phosphorus cod-liver oil had any action at all on acute rachitis. The most recent work of Towles and Schabad and Sorochowitsch indicates, therefore, that phosphorus cod-liver oil may not have any therapeutic action in the treatment of acute rachitis.

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40. Schabad: Phosphor. Lebertran und Sesamöl in der Therapie der Rachitis. Ihr Einfluss auf den Kalk-, Phosphor-, Stickstoff-, und Fettstoffwechsel. *Ztschr. f. klin. Med.*, 1909-10, lxix, 435.

41. Schabad and Sorochowitsch: Lipanin als Ersatzmittel des Lebertrans bei Rhachitis. Sein Einfluss auf den Stoffwechsel. *Monatschr. f. Kinderh.*, 1911, ix, 659.

oil with the addition of 6 per cent. oleic acid according to v. Mering,<sup>43</sup> as

42. v. Mering: Ein Ersatzmittel für Lebertran. *Therap. Monatsch.*, 1888, ii, 49.

43. Schabad and Sorochowitsch: Die Behandlung der Rachitis mit Lebertran-emulsionen und ihre Einwirkung auf den Stoffwechsel. *Monatschr. f. Kinderh.*, 1911, x, 12.

44. Towles, C.: Untersuchungen über den Einfluss des Phosphorlebertrans auf den Stoffwechsel eines rachitischen Säuglings. *Ztschr. f. Kinderh.*, 1910-11, i, 346.

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### ANATOMY, PHYSIOLOGY AND HYGIENE

- Baby-Tents of Chicago. F. W. Allin.  
Journal A. M. A., Dec. 30, 1911.
- Biologic Differentiation of Albuminoids in Milk. (Die biologische Differenzierung der Milcheiweisskörper.) H. Kleinschmidt.  
Monatschr. f. Kinderh., 1911, x, No. 8.
- Butter in Human Milk. (Etude du beurre dans le lait de femme par la centrifugation.) E. Plauchu and R. Rendu.  
Lyon Médical, Nov. 19, 1911.
- Clean Milk from Producer's Standpoint. H. E. Van Norman.  
Pennsylvania Med. Jour., December, 1911.
- Determination of Actual Size of Infants. (Ueber eine Methode zur Bestimmung des Volumens bei Säuglingen.) K. Oppenheimer.  
Ztschr. f. Kinderh., 1911, iii, No. 3.
- Development of Acidity in Cows' Milk and Its Relation to Time and Temperature. R. Vincent.  
Glasgow Med. Jour., December, 1911.
- Epidemic of Sore Throat Occurring in Boston and Vicinity During May, 1911. J. L. Goodale.  
Boston Med. and Surg. Jour., Dec. 14, 1911.
- Epidemic of Tonsillitis Due to Infected Milk. M. W. Richardson.  
Boston Med. and Surg. Jour., Dec. 14, 1911.
- Improved Medical Inspection of Public Schools and Its Results. G. J. Holmes.  
Jour. Med. Soc. New Jersey, December, 1911.
- Instruction of Teachers in School Hygiene. G. M. Whipple.  
Woman's Med. Jour., December, 1911.
- Medical Inspection in Public Schools, Its Needs and Desirabilities. A. B. Montgomery.  
Jour. Oklahoma Med. Assn., December, 1911.
- Medical Inspection in Toledo Public Schools. Its Aims and Some of Its Results. P. B. Brockaway.  
Am. Med. Compend, December, 1911.
- Medical Inspection of Schools. G. E. Hyde.  
Northwest Medicine, December, 1911.
- Medical Inspection of Schools. R. W. Jones.  
Wisconsin Med. Jour., November, 1911.
- The Menstrual Cycle, Its Physiology and the Preparation of the Young Girl for Its Advent. E. S. Brown.  
Woman's Med. Jour., November, 1911.
- Milk and Its Relation to Public Health. P. J. Eaton.  
Pennsylvania Med. Jour., December, 1911.
- Need of Medical Inspection of School Children in Ireland. O. S. Gogarty.  
Dublin Jour. Med. Sc., December, 1911.
- Outbreak of Tonsillitis or Septic Sore Throat in Eastern Massachusetts and its Relation to Infected Milk Supply. C. E. A. Winslow.  
Boston Med. and Surg. Jour., Dec. 14, 1911.
- Physiologic Differences Between the Cortex and the Medulla of the Thymus. (Bedeutung der eosinophil-gekörnnten Blutzellen im menschlichen Thymus.) H. Schridde.  
München. med. Wehnschr., Dec. 5, 1911.

- Physiology of Lactation. (Bedarf des physiologischen Reizes zur Anregung und Erhaltung der Laktation?) H. Helbich.  
Monatschr. f. Kinderh., 1911, x, No. 8.
- Preservation of Health in School Children. R. G. Freeman.  
Med. Rec., New York, Dec. 16, 1911.
- Sanitary Control of New York's Milk Supply. E. J. Lederle.  
Pennsylvania Med. Jour., December, 1911. Pediat., December, 1911.
- Tentative Classification of Exceptional Children. M. P. E. Crossmann.  
Cal. Jour. Med., December, 1911.

## PATHOLOGY AND BACTERIOLOGY

- Amyotrophy plus Obesity in Young Children; Two Cases. (Zur Frage der frühinfantilen Amyotrophie und einer sie begleitenden "endogenen" Fettsucht.) T. Gott and H. Schmidt.  
Ztschr. f. Kinderh., 1911, iii, No. 3.
- Atrophy of Certain Muscles as Cause of Lordotic Albuminuria. (Juvenile Dys-trophie und lordotische Albuminurie im Kindesalter.) E. Ebstein.  
Ztschr. f. Kinderh., 1911, iii, No. 3.
- Cancer of Ovary in Girl of Five. (Krebs des Eierstocks bei einem fünfjährigen Mädchen; Ovariectomie.) W. W. Rosanoff.  
Deutsch. med. Wchnschr., Dec. 14, 1911.
- Carcinoma and Sarcoma in Early Childhood. Q. W. Hunter.  
Pediat., December, 1911.
- Causes of Limping in Children. D. Savariaud.  
Med. Press and Circular, Dec. 13, 1911.
- Congenital Deformities of the Arms and Hands. (Ueber angeborene Verbildungen im Bereiche der oberen Extremität.) P. Glaessner.  
Deutsch. med. Wchnschr., Dec. 14, 1911.
- Cultural Studies on Mouth Spirochætæ. (*Treponema Microdentium* and *Macro-dentium*.) H. Noguchi.  
Jour. Exper. Med., January, 1912.
- A Dicephalic Monster. F. W. Bullen.  
Jour. Minn. Med. Assn., Dec. 15, 1911.
- Dull and Backward Children. A. F. Tredgold.  
Med. Press and Circ., Nov. 29, 1911.
- Large Umbilical Hernia, Containing Omentum, Gut and Liver, in Child Seven Months Old; Operation, Recovery. E. S. Allen.  
Kentucky Med. Jour., Nov. 15, 1911.
- No Basis for Assumption that Cretinism is Transmissible. (Zur Kontaktinfektion des Kretinismus.) A. Flinker.  
Wien. klin. Wchnschr., Dec. 21, 1911.
- Precociously Developed Male Pseudohermaphrodite. (Frühreifer Scheinzwitter.) R. Asch.  
Berl. klin. Wchnschr., Dec. 25, 1911.
- Reaction Curve in Glycerin Broth as Aid in Differentiating Bovine from Human Type of Tubercle Bacillus. M. Grund.  
Jour. Med. Research, December, 1911.
- Recent Studies in Experimental Pathology of Acute Anterior Poliomyelitis. P. A. Lewis.  
Pennsylvania Med. Jour., December, 1911.
- Recurrent Jaundice, Pyrexia, Splenomegaly, Anemia and Pigmentation of Skin in Girl Aged 11 Years. L. Guthrie.  
Practitioner, December, 1911.
- Relative Importance of Bovine and Human Types of Tubercle Bacilli in Different Forms of Human Tuberculosis. W. H. Park and C. Krumwiede.  
Jour. Med. Research, December, 1911.

- Research on the Stomach in Tetany in Children. (Magenuntersuchungen bei Kindlicher Tetanie.) F. Leist.  
 Monatschr. f. Kinderh., 1911, x, No. 8.
- Significance of Enlarged Lymph-Nodes in Children. G. K. Varden.  
 Atlanta Jour.-Rec. Med., December, 1911.
- Simultaneous Contrast Stain for Diphtheria Bacilli. (Eine neue einzeitige Doppelfärbungsmethode für die Polkörperchen der Diphtheriebazillen.) M. Raskin.  
 Deutsch. med. Wehnschr., Dec. 21, 1911.
- Spasms Nutans; Report of Four Cases. H. K. Hill.  
 Arch. Pediat., December, 1911.

### METABOLISM AND NUTRITION

- The Ash Content of the Muscles with Rachitis. (Ueber den Aschgehalt der Muskulatur bei Rachitischen.) E. Aschenheim and L. Kaumheimer.  
 Monatschr. f. Kinderh., 1911, x, No. 8.
- Breast Milk for Sick Infants. (Kranke Kinder bei Ernährung mit Frauenmilch.) L. Langstein and E. Hoerder.  
 Therap. Monatschr., December, 1911.
- Calcium Metabolism in Infantile Tetany, with Report of a Case. H. Schwarz and M. H. Bass.  
 Am. Jour. Dis. Child., January, 1912.
- Capillary Test of Viscosity of Milk. (Vergleichende Viskositätsbestimmungen der Milch mit Hilfe ihrer kapillären Steighöhe.) A. Kreidl and E. Lenk.  
 Wien. klin. Wehnschr., Nov. 30, 1911.
- Diabetes Mellitus in Childhood. W. Gellhorn.  
 Northwest Med., December, 1911.
- Fatal Case of Infantile Scurvy Following Diet Confined Almost Exclusively to "Grape Nuts." J. W. Amessee.  
 Denver Med. Times and Utah Med. Jour., December, 1911.
- Feeding of Children. D. E. English.  
 Jour. Med. Soc. New Jersey, December, 1911.
- Infant Feeding. C. H. Johnston.  
 Physician and Surg., November, 1911.
- Infant Feeding *Au Naturel*. S. Delano.  
 Boston Med. and Surg. Jour., Jan. 11, 1912.
- Nutrition and Metabolism. H. A. Milliken.  
 Jour. Maine Med. Assn., January, 1912.
- Nutrition of Children. S. F. Hale.  
 Southern Med. Jour., December, 1911.
- Practical Infant Feeding. A Study of 400 Cases. R. A. Benson.  
 Am. Jour. Obst. and Dis. of Women and Child., December, 1911.
- Quantitative Analysis of Human and of Cow's Milk. A. V. Meigs and H. L. Marsh.  
 Med. Rec. New York, Dec. 30, 1911.
- Recent Experiences in the Artificial Feeding of One Hundred Infants During the First Three Months of Life. F. C. Neff.  
 Jour. Am. Med. Assn., Dec. 23, 1911.
- Salvarsan in Scorbutus. (Ueber Salvarsanbehandlung bei Skorbut.) M. Tuschinsky and G. Iwaschenzow.  
 München. med. Wehnschr., Dec. 12, 1911.
- Splenomegaly (Gaucher). M. S. Reuben.  
 Am. Jour. Dis. Child., January, 1912.
- The "Split Proteid" Method of Artificial Feeding. W. D. Boggs.  
 Cal. Jour. Med., December, 1911.
- Studies on Infant Nutrition: II. The Hard or Casein Curds in Infants' Stools. A. M. Courtney.  
 Am. Jour. Dis. Child., January, 1912.



## DISEASES OF THE NEWLY BORN

- Congenital Fistulas in the Neck; Twenty-Three Cases. (Om medfødte halsfistler og endel med disse beslegtede anomalier.) F. Leegaard.  
Norsk. Mag. f. Lægevidensk., December, 1911.
- Congenital Imperforate Anus, with Occlusion of Entire Colon. C. H. Hamilton.  
Jour. Am. Med. Assn., Dec. 30, 1911.
- Fatal Jaundice of New-Born. Five Cases in One Family. J. N. Morris.  
Australian Med. Jour., Oct. 21, 1911.
- Glycocol in the Urine of New-Born Infants. (Vorkommen von Glykokoll im Harn des Neugeborenen.) A. v. Reuss.  
Ztschr. f. Kinderh., 1911, iii, No. 3.
- The Prematurely Born. (Quelques considérations sur les diverses variétés de prématurés.) A. Hergott.  
Ann. de gynéc. et d'obst., December, 1911.
- Resuscitation of Asphyxiated Infants by the Insufflation Method of Meltzer and Auer. E. Plauchu.  
Am. Jour. Dis. Child., January, 1912.
- Sepsis from Bednar's Aphthæ in New-Born Infants. (Sepsis bei Neugeborenen ausgehend von den Bednar'schen Aphthen.) G. Linzenmeier.  
Zentralbl. f. Gynäk., Dec. 16, 1911.
- Spina Bifida. B. B. Cates.  
Jour. Tennessee Med. Assn., December, 1911.
- Two Cases of Intracranial Cerebral Hemorrhage in New-Born Relieved by Operation. C. C. Simmons.  
Boston Med. and Surg. Jour., Jan. 11, 1912.
- The Ultimate Fate of the Prematurely Born. (Avenir éloigné du prématuré.) V. Wallich and A. Fruhinsholz.  
Ann. de gynéc. et d'obst., November, 1911.

## ACUTE AND INFECTIOUS DISEASES

- Acute Anterior Poliomyelitis. B. F. Green.  
Jour. Michigan Med. Soc., December, 1911.
- Acute Poliomyelitis: Diagnosis. D. Hecht.  
Interstate Med. Jour., December, 1911.
- Autoserotherapy in Infectious Diseases. P. Modinos.  
Presse méd., Dec. 6, 1911.
- Cancrum Oris. Case Following Typhoid Fever. J. R. Lockhart.  
Mississippi Med. Month., December, 1911.
- Case of Mild Anterior Poliomyelitis. W. N. Bullard.  
Boston Med. and Surg. Jour., Jan. 11, 1912.
- Cerebrospinal Meningitis as Recurrence After Salvarsan. (Zerebrospinalmeningitis als Rezidiv nach Salvarsan.) E. Oberholzer.  
München. med. Wehnschr., Dec. 12, 1911.
- Control of Measles. P. B. Brooks.  
Med. Rec., New York, Dec. 23, 1911.
- Diagnosis and Medical Treatment of Poliomyelitis. W. G. Spiller.  
Pennsylvania Med. Jour., December, 1911.
- Diphtheria Antitoxin and Anaphylaxis. J. A. Roddy.  
New York Med. Jour., Dec. 16, 1911.
- Diphtheria Carriers and Medical Inspection of Schools. H. Albert.  
Iowa Med. Jour., December, 1911.
- Epidemic Anterior Poliomyelitis in South Derbyshire. J. H. Moir.  
British Med. Jour., Dec. 30, 1911.
- Epidemic Paralysis in Hampshire. G. F. England.  
British Med. Jour., Dec. 30, 1911.
- Epidemic Poliomyelitis. A. D. Young.  
Jour. Oklahoma Med. Assn., December, 1911.

- Epidemic Poliomyelitis. L. W. Rork.  
Western Med. Rev., December, 1911.
- Epidemic Poliomyelitis Occurring at Stowmarket, Suffolk. S. Hillier.  
Brit. Med. Jour., Dec. 30, 1911.
- Experimental Research on Acute Poliomyelitis. II. (Maladie de Heine-Medin.)  
K. Landsteiner, C. Levaditi and M. Pastia.  
Ann. de l'Inst. Pasteur, November, 1911.
- The Kidney in Scarlet Fever. (Zur Frage der Scharlachnephritis.) (C. Leede.  
München. med. Wehnschr., Nov. 28, 1911.
- Pennsylvania's Work on Poliomyelitis. S. G. Dixon.  
Pennsylvania Med. Jour., December, 1911.
- Poliomyelitis. T. M. Koon.  
Jour. Michigan Med. Soc., December, 1911.
- Practical Points in Diagnosis and Treatment of Diphtheria. A. Levinson.  
Med. Record, Jan. 6, 1912.
- Prophylaxis and Treatment of Infantile Paralysis. J. W. Amesse.  
Pediat., December, 1911.
- Prophylaxis of Infectious Diseases in Infant Wards. (Die Verhütung und Bekämpfung der Infektionskrankheiten in geschlossenen Säuglingsanstalten.)  
J. Cassel.  
Deutsch. med. Wehnschr., Nov. 30, 1911.
- Rheumatism in Children. T. M. Anderson.  
Am. Jour. Obst., December, 1911.
- Smallpox and Chickenpox. H. W. Hill.  
Journal-Lancet, Jan. 1, 1912.
- Treatment of Diphtheria Carriers by Overriding Infected Area with Culture of Staphylococcus Pyogenes Aureus. H. Page.  
New York Med. Jour., Dec. 23, 1911.
- Two Cases of Poliomyelitis Mistaken for Neuritis. T. A. Williams.  
Boston Med. and Surg. Jour., Jan. 11, 1912.
- Unusual Case of Typhoid in Young Girl. F. J. Barrett.  
Med. Rec., New York, Dec. 16, 1911.

#### TUBERCULOSIS AND SYPHILIS

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Bristol Med.-Chir. Jour., December, 1911.
- Present Status of Our Knowledge of Infectiousness of Milk Containing Tubercle Bacilli. P. C. Heinemann.  
Illinois Med. Jour., December, 1911.
- Prognosis of Tuberculosis in Young Infants. (Zur Prognose der tuberkulösen Infektion im frühen Säuglingsalter.) J. Ibrahim.  
Beitr. z. Klin. d. Tuberk., 1911, xxi, No. 2.
- Syphilis as Factor in Abnormal Development of Children. E. W. Dittrich.  
Am. Jour. Obst., January, 1912.
- Tubercular Laryngitis in Infant of Seventeen Months. J. M. Hunt.  
Med. Press and Circular, Dec. 6, 1911.
- Tubercular Peritonitis in Children with Special Reference to Fibrous Form. J. M. Acker.  
Mississippi Med. Month., December, 1911.
- Tuberculin Reactions and Their Comparative Value as Diagnostic Aids. O. H. Benker.  
Interstate Med. Jour., December, 1911.

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Arch. Pediat., December, 1911.

- Care of Children's Teeth. J. L. Austin.  
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- Infantile Hypertrophic Stenosis of Pylorus, Based on Seven Operated Cases. F. E. Bunts.  
 Am. Jour. Med. Sc., January, 1912.
- Molds in Alimentary Canal. I. P. Hall.  
 Canadian Med. Assn. Jour., December, 1911.
- Pyloric Stenosis in Infants. J. B. Bilderbach.  
 Med. Sentinel, December, 1911.
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 Arch. Pediat., December, 1911.
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 Clinical Journal, Nov. 22, 1911.
- Chorea of Genital Origin. (Chorea genitalen Ursprunges.) L. M. Bossi.  
 Zentralbl. f. Chir., Dec. 9, 1911.
- Management of the Nervous Child. M. L. Perry.  
 Jour. Kansas Med. Soc., November, 1911.
- Meningeal and Cerebral Symptoms in Infants. (Meningeale und cerebrale Krankheitsbilder beim Neugeborenen und Säugling.) W. Knöpfelmacher.  
 Med. Klinik, Dec. 24, 1911.
- Nervous Diseases in Children. J. P. Parkinson.  
 Clinical Journal, Nov. 29, 1911.
- Nervous Manifestations in Children and Their Treatment. R. O. Moon.  
 Med. Press and Circ., Dec. 20, 1911.
- Overfeeding and Convulsions. (Ueberfütterung und Krämpfe.) E. Ebstein.  
 Ztschr. f. Kinderh., 1911, iii, No. 3.
- The Recognition of the Pre-Neurasthenic and Pre-Insane Condition in the Young.  
 A Study for the General Practitioner. R. Moore.  
 Jour. Am. Med. Assn., Dec. 23, 1911.
- Report of Brain Cases. W. J. Butler.  
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#### GENITO-URINARY SYSTEM

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 Lancet, Dec. 9, 1911.
- Primary Pyelitis in Infants. J. T. Fotheringham.  
 Canadian Med. Assn. Jour., December, 1911.

Treatment of Gonorrheal Cervicitis. (Zur Behandlung der Cervicalgonorrhoe.)  
Wagner.

Berl. klin. Wechnschr., Dec. 25, 1911.

Venereal Diseases and Their Relation to Infant Mortality and Race Deterioration.  
P. A. Morrow.

New York Med. Jour., Dec. 30, 1911.

#### EYE, EAR, NOSE AND THROAT

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Cases of Late Secondary Hemorrhage after Tonsillotomy. F. E. Hopkins.

Ann. of Oto., Rhin. and Laryng., September, 1911.

Cases of Night-Blindness with Peculiar Conjunctival Changes in Children. S. Stephenson.

Brit. Jour. Child. Dis., December, 1911.

Civic Medical Inspection of School Children, With Special Reference to Diseases of Eye, Ear and Throat. S. C. Ayres.

Lancet-Clinic, Dec. 23, 1911.

Clinical Aspects of Epidemic of Septic Sore Throat in Cambridge, May, 1911. E. A. Darling.

Boston Med. and Surg. Jour., Dec. 14, 1911.

Complications Following Tonsillectomy. I. A. Lederman.

Kentucky Med. Jour., Dec. 15, 1911.

Condition of Nose, Throat and Ear as Factor in Exceptional Development. O. Glogau.

Am. Jour. Obst., January, 1912.

Indications for and Method of Removal of Tonsils. J. A. Duff.

West Virginia Med. Jour., December, 1911.

Multiple Papillomata of Larynx in Children. E. C. Sewell.

Cal. Jour. Med., January, 1912.

Phase of Tonsil Question. R. W. Perry.

Northwest Med., December, 1911.

Postoperative Tonsillar Hemorrhage. J. E. Sawtell.

Jour. Kansas Med. Soc., November, 1911.

Relation of Enlarged Tonsils to Endocarditis. A. C. Getchell.

Ann. of Oto., Rhin., and Laryng., September, 1911.

Some Popular Misconceptions Regarding Ophthalmia Neonatorum. E. M. Alger.

New York State Jour. Med., December, 1911.

Strabismus. (Ueber Entstehung und Behandlung des Schielens.) C. Adam.

Med. Klin., Dec. 17, 1911.

Technic of Tonsillectomy. J. M. Ingersoll.

Ann. of Oto., Rhin., and Laryng., September, 1911.

Tonsils in Pathology. (Die Tonsillen als Eintrittspforte der Infektionskrankheiten.) G. Finder.

Med. Klin., Dec. 10, 1911.

Tonsil Instruments. R. J. Tivnen.

Illinois Med. Jour., December, 1911.

Why Re-Operate in Adenoids? G. W. Spohn.

Jour. Indiana Med. Assn., December, 1911.

#### SURGERY

Certain Operative Procedures in Paralysis of Children. R. Jones.

British Med. Jour., Dec. 9, 1911.

Pin in Bronchus—Report of a Case. F. G. Hodgson.

Atlanta Jour.-Rec. Med., December, 1911.

A Point in the Treatment of Lateral Curvature of the Spine. E. A. Rich.

Jour. Am. Med. Assn., Dec. 30, 1911.

- Simple Appliance for the Relief of Residual Peroneal Paralysis Following Acute Anterior Poliomyelitis. C. O. Griffin.  
Therap. Gaz., December, 1911.
- Surgery and Electro-Therapeusis in Infantile Paralysis: Attempt to Define Sphere of Each.  
British. Jour. Child. Dis., December, 1911.
- Surgical Treatment of Poliomyelitis. G. G. Davis.  
Pennsylvania Med. Jour., December, 1911.

# MISCELLANEOUS

- Backward Child vs. the Feeble-Minded Child. M. P. E. Groszmann.  
Am. Jour. Obst., January, 1912.
- Care of the Crippled and Rachitic in Italy. D. C. McMurtrie.  
Med. Rec., New York, Dec. 16, 1911.
- Clinical Studies of Exceptional Children. E. B. McCready.  
Am. Jour. Obst., January, 1912.
- Common Ailments in Infancy and Their Treatment. E. Pritchard.  
Pediat., December, 1911.
- Etiologic Factors in Exceptional Children and Their Prevention. M. Neustaedter.  
Am. Jour. Obst., January, 1912.
- Progressive Methods of Dealing with Juvenile Delinquency. N. B. Neelen.  
Am. Jour. Obst., January, 1912.
- Providing for Crippled Children. C. J. Cook.  
Lancet-Clinic, Dec. 9, 1911.
- Social and Moral Considerations Related to Medical and Surgical Care of Crippled Children. D. C. McMurtrie.  
New York Med. Jour., Dec. 30, 1911.
- Speech Defects in Children. J. M. Fletcher.  
Am. Jour. Obst., January, 1912.
- Unnecessary Infant Mortality. G. H. Irvin.  
Cleveland Med. and Surg. Reporter, November, 1911.
- Value of Physical Activities in Treatment of Atypical Boys. G. Meylan.  
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## THE USE OF A SIMPLE DUODENAL CATHETER IN THE DIAGNOSIS AND TREATMENT OF CERTAIN CASES OF VOMITING IN INFANTS \*

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Some months ago I described in the pages of this journal<sup>1</sup> a duodenal tube for infants. This tube was introduced by mouth into the stomach, and then passed through the pylorus into the small intestine. This result was readily accomplished, the tube taking about one-half hour to pass the pylorus. The radiographs which accompanied this article showed conclusively that the end of the tube lay in the duodenum, and was not merely curled on itself within the stomach cavity. This duodenal tube, in brief, consisted of soft rubber tubing with a silver-plated, perforated leaden ball at the end, and was a modification of the Gross duodenal tube used for adults. By means of this simple device, I was able, after some practice, to gain access to the duodenum in infants in almost every instance, and gradually acquired increased facility in its use. This was, I believe, the first conclusive proof that the intestine could be reached by this route in infancy. The principle involved in this manipulation was that of gravity, carrying the leaden ball to the pylorus, aided by the onward movement of peristalsis, which swept the ball through the pyloric ring, and thence into the intestine. Although this tube served its purpose, I have laid it aside for one which is simpler, as well as more serviceable, and which has afforded me a ready means of studying the functions of the stomach and intestines from a new point of view.

In the course of my experiments it occurred to me to try whether I could obtain the same result by making use of the ordinary soft rubber Nélaton catheter, which is used so frequently in infants and in adults for the purposes of lavage and feeding. To my gratification and surprise I found that this simple instrument can be passed readily from the stomach

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<sup>1</sup>Read at the meeting of the New York Academy of Medicine, Pediatric Section, Dec. 14, 1911.

1. Hess, A. F.: A Duodenal Tube for Infants, *AM. JOUR. DIS. CHILD.*, May, 1911, p. 360.

into the duodenum. It is indeed interesting and instructive to reflect on the fact that this catheter, which was introduced into the realm of pediatrics by Epstein in 1880 for the purpose of gastric feeding and

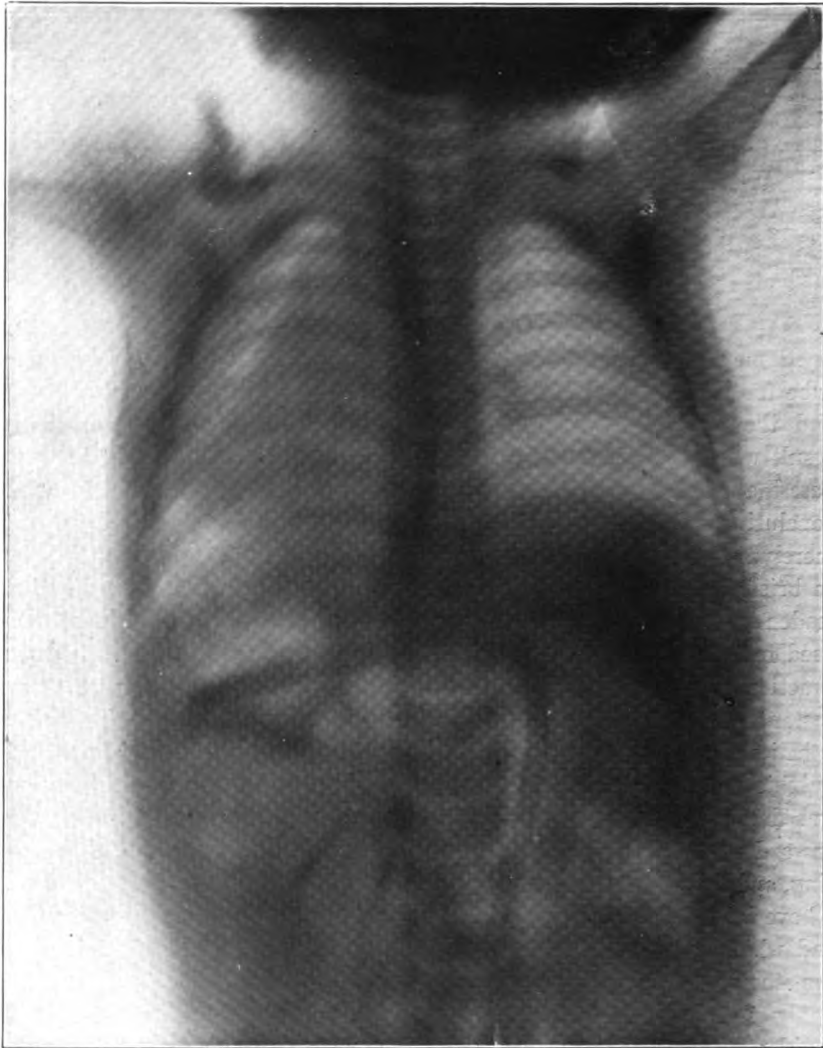


Fig. 1.—View from posterior showing catheter well within the duodenum. Note the sharp turn to the left, to the fundus, which the catheter invariably takes on entering the stomach.

investigation, has, in these many years, never been seriously thought of in connection with the diagnosis and treatment of pyloric conditions and of intestinal disturbances, subjects which have been considered of primary importance during this long period.



During the past few months I have made use of this catheter, which may in this connection be termed an "infant duodenal catheter," for these purposes on more than 200 infants of various ages, suffering from a great variety of disorders, and can at this time speak with confidence of its practicability in this connection.

In order to demonstrate beyond all doubt that the catheter gains



Fig. 2.—View from the anterior of a duodenal catheter deep in the duodenum.

access to the duodenum, I have once more resorted to radiographic pictures (Figs. 1 to 4), criteria which are least open to doubt, and which have enabled me to prove this point conclusively. From these pictures, for which I take pleasure in thanking Dr. Hirsch, it will be seen that the tube is well within the intestine; in fact, in one instance, seems to have passed even beyond the confines of the duodenum. It will be noted also that the catheter does not take a direct course from the cardiac end

of the stomach to the pylorus, but that just as in the case of the duodenal tube, which I previously described, the catheter on entering the stomach cavity makes a sharp bend to the left to the fundus, and then turns

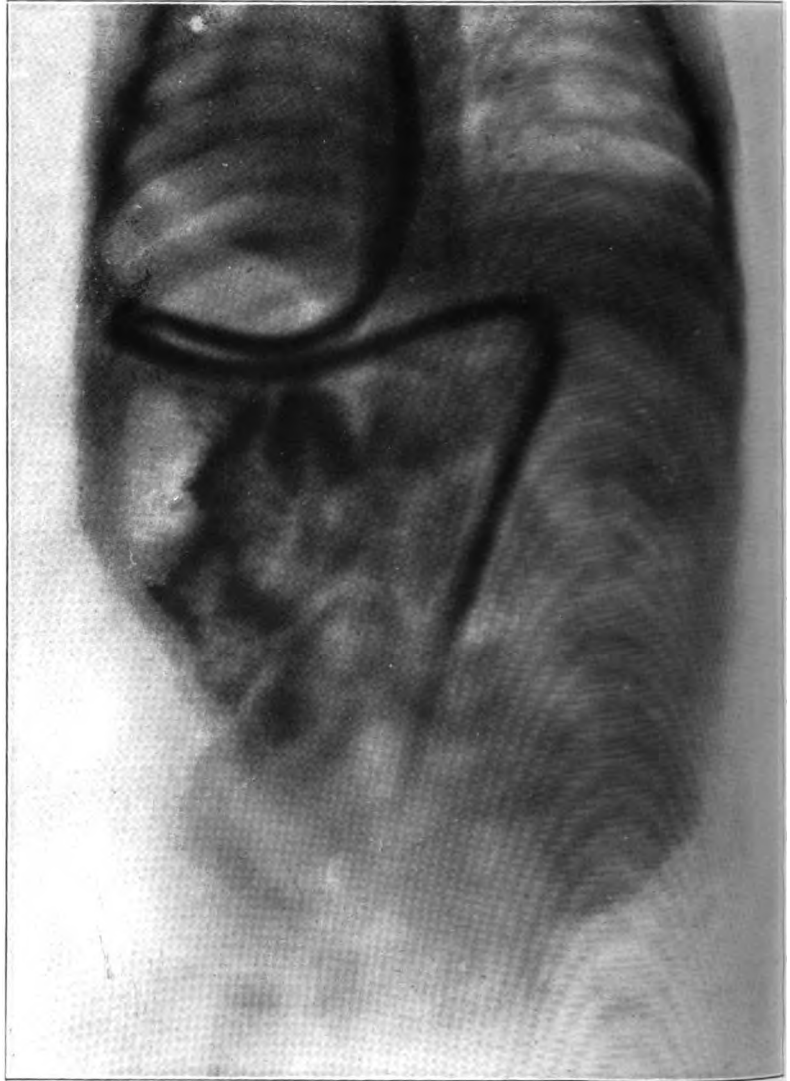


Fig. 3.—View from posterior. Duodenal feeding of 3-months-old infant; stomach empty; bismuth-milk mixture in coils of intestine.

itself to the right to reach the pyloric opening. This has been the course followed in all radiographs which I have had taken, either of this catheter or of its predecessor, the duodenal tube. This novel and unexpected picture controverts the assumption which I first considered, to explain the

ease with which I was able in infants to reach the pylorus. It shows that this success cannot be attributed to the vertical position of the stomach in infancy, nor to the fact that the tube or catheter follows an

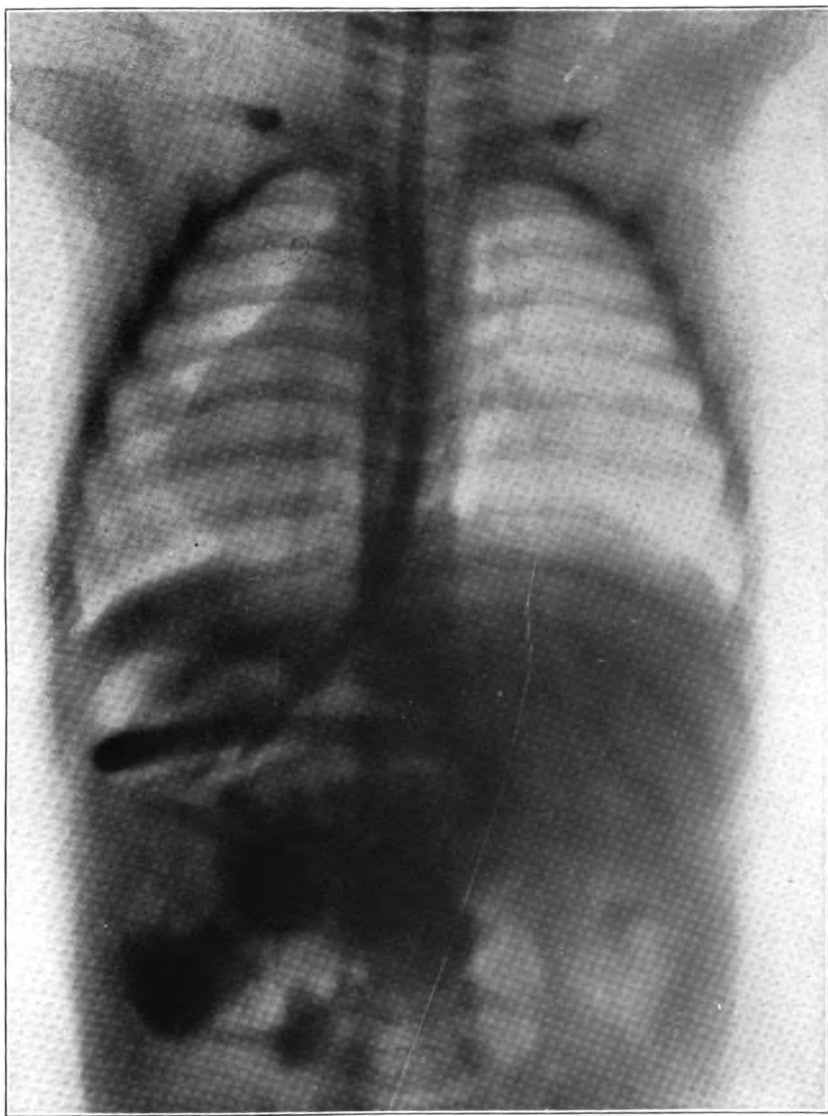


Fig. 4.—Duodenal feeding. M. C., 9 months old. Catheter and bismuth in the duodenum; stomach empty. View from the posterior.

almost vertical course in its route to the small intestine, and has led me to attribute the success of the procedure rather to the diminutive size of the stomach cavity, and also perhaps to a relative lack of tonicity of

the pyloric ring. This explanation gains added weight from the fact that a catheter of this kind cannot be used for this purpose in the adult, in whom the stomach is large, and the tube wanders far from the pyloric opening.

#### TECHNIC

It is difficult to describe the method of use of this simple instrument, for like all other instruments, even of a simple nature, its use can be learned only with some practice, and the descriptions are far more complicated than the procedure would warrant. For the purpose an ordinary No. 15 (F.) soft rubber catheter should be employed, preferably one with a large eye; if the baby is very small, under a month of age, a No. 14 (F.) catheter should be made use of. Before beginning we should designate points 20, 25 and 30 cm. distant from the eye. This can be done by means of pen and ink. These markings allow us to take our bearings while introducing the catheter, and as long as it is in place. The catheter is now ready for use. The only other instrument necessary is an aspirator; for this purpose either the same aspirating bulb which I described in my previous article may be used, or an ordinary aspirating syringe. The instrument is now complete. The physician, therefore, generally has an infant duodenal catheter at hand, and needs but to acquaint himself with its use.<sup>2</sup>

The catheter is passed in the same way as the ordinary stomach tube. that is to say, it is lubricated with water, introduced into the mouth, and without the aid of the finger is rapidly pushed down the pharynx and esophagus into the stomach. It has seemed immaterial to me whether the baby is held in the sitting position, or lies on its back, or on the side. I have generally had it placed on its back with the arms bound snugly to its side by means of a towel. In a baby 2 months old, for example, when the 20 cm. mark is about 3 or 4 cm. from the gums, the contents of the stomach begin to be evacuated. This food is generally acid, and may contain free hydrochloric acid, as shown by its reaction to congo paper, if the feeding has been given some hours previously. After the stomach is empty, if we insert the catheter gently a little further, we

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2. Although a serviceable instrument can be prepared in this way by anybody wishing to make use of one, and a great deal of my work was carried out by means of a catheter which I happened to have on hand, nevertheless a catheter with two eyes at the tip, of exceptional length, and carefully marked, has additional advantages. The use of the bulb instead of an ordinary aspirating syringe has decided advantages, the greatest is that in aspirating through the bulb by means of the mouth one can in this way appreciate the amount of resistance offered by the stomach, or intestine, and thus gain valuable information as to the whereabouts of the end of the catheter. I should by all means urge anyone who intends to use this method frequently to make use of an aspirating bulb. The bulbs and the infant duodenal catheters may be obtained of Tiemann & Co., New York.

shall find no resistance until the 20 cm. mark is about at the gums, when a sense of obstruction may be felt, and the infant may gag, due to the contact of the end of the tube with the pylorus. While there is gagging or crying, accompanied by forced expiration, the tube should never be advanced, for at this time the pyloric valve, and indeed the cardia as well, is constricted and prevents further passage. If we push on a little until we reach the 25 cm. mark, we shall in most cases by this simple means have gained access to the duodenum. Indeed I have no doubt, and a recent perusal of the literature has confirmed me in this opinion, that many have reached the intestine when they wished merely to enter the stomach, and I believe that numerous reports which are supposed to record the capacity of the stomach, or to describe the nature of its contents, in reality combine data of the contents of this viscus and that of the upper part of the small intestine as well. When we consider also that pressure of the tip of the catheter on the pylorus at times causes the pyloric valve to allow duodenal contents to pass into the stomach, there is further reason for believing that errors have crept in.

Naturally, the first question is "How do we know that we have reached the intestine, and why may not the catheter be curled on itself within the stomach?" Indeed it is far easier to enter the duodenum than to learn the phenomena by which we may judge whether or not we are in the intestine; however, the more experience we gain the easier it becomes to judge of this point, and for some time I have felt very little uncertainty in this regard. There are several ways of ascertaining this fact. In the first place we must have an approximate knowledge of the distance of the pylorus from the gums or teeth. For example, this measurement for clinical purposes is about 20 cm. at one month, gradually increasing to about 25 cm. at a year.

Let us suppose that we are passing the duodenal catheter on a baby 3 months of age, and that we have gradually inserted it to the 25 or 30 cm. mark. We then halt, and watch to see whether the tube has a tendency to remain at this level or not. If you push a tube into the stomach, and have it coil up within its cavity, it will almost always, sometimes quickly, sometimes more slowly, the time depending on the fact of whether the child is quiet, or gags and resists, work its way out of the mouth, so that the 20 cm. mark comes into view again. If, however, the tube has passed into the duodenum and is held by the pyloric sphincter, it will project almost vertically from the mouth and have a tendency, unless there is marked gagging, to hold its position, and not to work its way out again. This is an important, although not pathognomonic sign of having reached the intestine. Frequently we are aided in obtaining our bearings by feeling the grip of the pylorus, an intermittent closure, when we pull slightly on the catheter.

It might be thought that one of the most useful tests for orientation would consist in obtaining alkaline fluid or bile on aspiration, and most certainly if we obtain such fluids the evidence of success is convincing, and the gratification proportionately great. However, unless we are prepared to spend one-half hour, or an hour, or at times a still longer period, we may be unable to demonstrate our success in this manner. Nor is this necessary. The duodenal contents are frequently acid, and may continue to be so, due to the fact that gastric juice is being poured out into the stomach and thence into the intestine. This may render it impossible to obtain alkaline juice, although the fluid may be golden yellow due to bile, and contain the various pancreatic ferments. Moreover we may obtain a neutral or alkaline juice without any bile, as the bile is excreted intermittently, and often at long intervals, so that if we were to depend entirely on the reaction of the fluid or on its bile content, in judging of our success in reaching the intestine, we would often consider ourselves unsuccessful, whereas in reality we had reached the desired goal.

A test which is of value, especially in the beginning of the use of the catheter, is what I have called for the sake of brevity the "retraction test." By this I mean that when we are in doubt as to whether the catheter is in the stomach or duodenum, we retract it very slowly, having an assistant aspirate through the bulb as we do so, until we have reentered the stomach cavity. In this way, if the catheter has been withdrawn from the duodenum, one of two signs may be noted: either the assistant may note a marked change of resistance to aspiration, as the end of the catheter leaves the small constricted intestinal cavity and enters the stomach (and indeed frequently the assistant may give the first signal that the tube has left the intestine), or it may be noted by the sudden change in the nature of the juices obtained. Whereas, when the tube was in the duodenum a small amount of viscid fluid, neutral or somewhat acid, was being aspirated, or indeed no fluid could be obtained, when the tube is withdrawn to, let us say, the 20 cm. mark, suddenly there is a noisy gush of fluid of an entirely different nature, perhaps containing a marked admixture of foamy saliva, generally much larger in quantity, and frequently far more acid than that which had been obtained in the duodenum. As I have said, this test tells us whether the catheter was in the duodenum or not; however, it necessitates our making a second attempt to pass the pylorus. The more we use the tube the less we have to resort to this test.

Another test, but one of much less value, is what I have termed the "papillary bile-test." By this I mean that sometimes when we withdraw the tube from the intestine toward the stomach, and reach the level of the papilla of Vater, there is a sudden gush of bile-stained fluid. This, however, is not usually the case, and the test cannot be relied on, but

should be remembered, and made use of, in case this sign is noted in the course of the "retraction test."

Like most manipulations the passage of the duodenal catheter requires some practice and cannot be learned by description, but only by personal experience. I have found that after a few attempts the technic was fairly well acquired by hospital interns. The simplest method of acquiring the technic is to pass the catheter in the way described, and control the result by means of the fluoroscope (the catheter casts a deep shadow without the aid of bismuth). However, the x-ray is by no means necessary, and I did not make use of it in gaining my experience. Practice — far less practice than is required to master the technic of an otologic examination — is all that is required. Indeed in very young infants it is difficult not to enter the duodenum if we do not push the catheter forward with too great haste. The younger the infant the easier is this accomplished. I have passed the catheter without difficulty on infants ranging in age from a few hours to one and one-half years. However, in a broad sense it may be stated that the younger the infant the easier it is to transgress the pyloric barrier.

In this paper in addition to describing a simple method of reaching the intestine in infants, a technic which seems to me to offer additional possibilities for diagnosis, for therapeutics and for physiologic experiment, I wish to describe how this procedure has been of value in the diagnosis and treatment of some pathologic conditions which I have encountered during the past few months.

#### THE CATHETER IN DIAGNOSIS

Let us consider the subject of diagnosis. There is perhaps no group of cases more puzzling at times than that characterized by persistent vomiting. From day to day our diagnosis wavers among various possibilities — chronic indigestion, pyloric spasm, beginning pyloric stenosis and other less common and even less well defined conditions thrust themselves forward in turn for consideration. For although the diagnosis in the classical case is simple, in many others we grope for weeks, and even when all is over we do not feel confident that we have solved the nature of the disturbance. In cases of this description the duodenal catheter, and at times the soft rubber ball-tube as well, has been of assistance. To cite an instance:

CASE 1.—A. W., aged 2 months, weight 5¼ pounds, a premature baby, with a history of vomiting for some weeks, was admitted to Dr. Caillé's service at the Post Graduate Hospital, May 10, 1911. After admission the infant regurgitated almost all feedings; temperature was subnormal, stools yellow. Food consisted of a milk-mixture containing approximately 1 per cent fat, 6 per cent. sugar, 1 per cent. protein, of which 3 ounces were given every three hours.

May 13, 4 p. m. Catheter passed and stomach emptied of about ½ ounce of watery fluid. Some difficulty in passing tube into stomach. Duodenum could

not be entered. The duodenal ball-tube (6 mm. ball) was also tried without success. Both were held at the 20 cm. mark.

At 4:25 p. m. an attempt was made to allow the tube to find its way through the pylorus by the slow method, by peristalsis. The cardia, and more especially the pylorus, seemed irritable, the baby crying when the tube was pushed beyond 20 cm. mark. Five c.c. of markedly acid juice was obtained. At 5:30 water was put into the stomach to aid instrumentation, but of no avail; held always at 20 cm. mark. At 5:35 the tube was removed.

**Epicrisis:** A case of spasm or stenosis of the pylorus, combined with spasm of the cardia. Nothing was known of the history of vomiting of this case when the catheter was passed, as the infant was selected for the purpose of obtaining duodenal juice for chemical examination. It was only after our unexpected failure to pass the pylorus that we inquired the anamnesis, and learned to our great interest of the persistent vomiting. We then put 4 ounces of fluid into the stomach by lavage, but no marked gastric peristalsis was noted; 1 ounce of this fluid was forcibly ejected.

May 16, Test 2: Baby still regurgitates; food the same; fed two hours ago; temperature subnormal; stool yellow.

3:30 p. m., 6 mm. ball-tube passed; obstruction at 15 cm., which was overcome; marked acidity of food in stomach; ball again held at about 21 cm. mark, even though water was put into stomach (accessory method).

4:05, tube withdrawn, some obstruction at cardia.

4:10, 16 (F.) catheter passed, slight obstruction at 15 cm.; marked obstruction at pylorus.

4:35, marked gastric secretion; ball-tube again tried, after dipping it into cod-liver oil and pouring a small amount of oil into stomach. Failure.

**Epicrisis:** Again failure to enter duodenum, obstruction at cardia and at pylorus as previously noted.

May 18, Test 3: Child has vomited less since last passage of tube. Is getting mixture of milk containing approximately 2 per cent. fat, 6 per cent. sugar, and 1 per cent. proteids.

4:15, No. 12 (F.) catheter introduced into stomach, and a small quantity of very acid Congo + fluid evacuated. Obstruction at cardia at 15 cm. noted as previously.

4:45, Tube reintroduced, and at once golden, faintly alkaline fluid was obtained; 8 c.c. aspirated with the tube introduced 22 to 27 cm. (This fluid was found to contain the pancreatic ferments, amylase, protease, and lipase in considerable amounts.)

5:10, Tube removed. Pylorus probably at 21 cm. level.

5:30, 6 mm. ball-tube introduced. This could not be advanced beyond the cardia without having the baby swallow water. In 10 minutes it did not pass the pylorus.

**Epicrisis:** At the third test we were able to enter the duodenum, as proved by aspirating bile, and a large quantity of fluid containing all the pancreatic ferments. The pathologic condition in this case, therefore, would seem to have been a spasm of the pylorus and cardia, rather than an organic stenosis. If a stenosis did exist, it could not have been present to a marked degree.

May 27, Test 4: Baby still vomiting repeatedly. Six mm. ball-tube passed through the cardia and the pylorus by means of having the baby swallow water (accessory method). Bile obtained, and a large amount (6 c.c.) of pancreatic juice containing the three ferments. In duodenum thirty minutes.

June 1, Test 5: Baby still has propulsive vomiting. Six mm. ball-tube passed with difficulty (accessory method); a marked grip of the pylorus noted; bile obtained; tube then withdrawn.

June 9, Test 6: Infant had been given paregoric to stop the vomiting, but without effect. Condition very poor. Weight 4 pounds, 12 ounces.

4:30, 6 mm. tube passed through pylorus, by the aid of water, as proved by the "retraction test."



4:55, reintroduced. Two ounces of milk-mixture fed slowly into duodenum.

June 10, Test 7: 10 a. m., inserted tube into duodenum again; 11 a. m., 8 c.c. of bile-colored fluid obtained in one hour. This fluid was alkaline, and contained the three pancreatic ferments. Pyloric tugging marked when tube was withdrawn from duodenum.

In all, seven tests were carried out on this infant. In the first two attempts we were unable to pass the catheter into the intestine. In the others this was accomplished with difficulty, and only by the aid of introducing water into the stomach. This technical resort is often very helpful, as the pylorus relaxes to allow the water to pass through, and in this way the catheter also obtains access to the duodenum. For the sake of brevity, this device, for which we do not claim originality, has been referred to in the notes as the "accessory method." In this case where a spasm of the cardia as well as of the pylorus existed, this method proved especially helpful in relaxing both sphincters. It is of interest to note that in addition to the increased amount of gastric secretion which has so frequently been observed in conjunction with pyloric spasm, there was in this case, as evidenced in the second and third test, an increased flow of pancreatic secretion as compared with the amount usually obtained. At the time this case presented itself for examination we had just begun to use the duodenal catheter, and were still employing the ball-tube. It is very probable that had we used the catheter in the examinations we should have been able to enter the duodenum more readily.

We were not in a position to attempt systematic duodenal feeding of this infant; however, the one attempt made at the time of the sixth test showed that this was feasible, and it is to be regretted that the baby could not have been given alimentation continuously by this route.

It is not our purpose to give in detail an account of all the cases of pylorospasm which we have tested by means of the duodenal catheter, nor, indeed, to discuss in this place the nature and peculiarities of this interesting condition. We have passed the catheter on numerous infants, who on account of persistent vomiting were suspected to be suffering from this condition. In many of these cases the catheter was readily passed to and fro between the intestine and the stomach, so that the diagnosis of spasm could readily be set aside. On others a definite obstruction was encountered. One of these has specific points of interest, and, therefore, may well be recounted in detail:

CASE 2.—M. S., 3 months of age, with marasmus; never nursed; had vomited a great deal between June 27 and July 20. Gavage and paregoric used. Not vomiting at present. Weight 4 pounds, 5 ounces. Fed every two hours, 3 ounces of a mixture containing one-half boiled milk, one-half water, and 5 per cent. sugar; had been fed two hours previous to test, which was carried out to obtain pancreatic ferments.

August 18, Test 1: 2:20, catheter introduced into stomach, which was found to be empty. 2:25, No. 14 (F.) catheter passed readily into duodenum. Some warm water was given. In the course of thirty minutes about 13 c.c. of alkaline, greenish, slightly viscid fluid was obtained (subsequent examination showed this to contain lipase and protease to a marked degree; the amylase test was lost). 12:55, tube removed. Clear acid fluid obtained in stomach.

Epicrisis: A normal case except for the excessive secretion of duodenal fluid.

September 12, Test 2: Weight 4 pounds, 8 ounces. Appears nervous and cries a great deal. Since September 3 infant has been vomiting, and for the past three days has vomited all food. It is given 4 ounces of skimmed milk every two hours. For the past twenty-four hours the infant received 4 minims of paregoric every four hours, as from July 12 to July 17; was fed about two hours previous to test. 2:20, No. 14 (F.) catheter passed. Stomach empty. 2:35, catheter again passed into stomach. Same obstruction at cardia, which was passed; the sphincter was felt to grip the catheter when withdrawal was attempted. Could not pass the pylorus even with the aid of the "accessory method." Marked flow of gastric juice, giving a strong reaction for free hydrochloric acid (Congo).

3:40, Catheter removed. Grip of cardia again clearly felt on withdrawal.

Epicrisis: Spasm of cardia and pylorus with marked gastric secretion.

September 15, Test 3: Weight 4 pounds, 15 ounces. Regurgitates much less. Has gained 7 ounces in four days. Still obtains paregoric in same doses. No 16 (F.) catheter at once passed into duodenum and bile obtained. Child much quieter.

Here we have the record of a child which gave a history of vomiting during the second month of life, but when examined in the third month seemed normal, as far as our test is concerned, except for an excessive duodenal secretion. About two weeks later it began again to regurgitate persistently, and when tested for a second time gave unmistakable signs of cardiospasm and pylorospasm. The spastic condition developed under our observation. A third passage of the catheter, carried out a few days later, revealed the fact that the spasms had relaxed, and coincident with this change in physical condition, a decided decrease in the regurgitation was noted, as well as a general improvement and gain in weight. This improvement took place subsequent to the passage of the catheter. However, in spite of the fact that it retained its food it gradually sank, and died of marasmus about two weeks later. Duodenal feeding was not attempted, as there was no one at hand to carry it out satisfactorily.

It will be seen from a survey of these two cases, and I may add that other instances corroborate this view, that the duodenal catheter enables us to make an absolute diagnosis of pyloric spasm, and to sharply differentiate this condition from vomiting not spastic in nature. A single test generally has been sufficient to draw this distinction. However, if we merely fail to enter the duodenum in a case, we would certainly err to attribute this failure to spasm. But if we are sure of our technic, and have passed the catheter in numerous instances without difficulty, and then meet with a case offering persistent obstruction at the level of the pylorus, we are justified in attributing this hindrance to pyloric spasm. This can be our conclusion only if we finally overcome the obstruction.

If we fail to enter the intestine, a single test must be considered insufficient, as the failure may be due to other causes, especially if our experience has not been wide. It is in such cases as I have detailed at length, in which the catheter is repulsed again and again at the same level, where we finally feel the resistance give way and the catheter pass, where there is a marked grip or tugging when the attempt to retract is made, that we may venture a diagnosis of spasm. It is not possible to differentiate between a simple spasm and a true stenosis of so mild a grade that it permits of the passage of a No. 15 (F.) catheter. However, if we are unable to enter the intestine after repeated attempts in the case of an infant showing symptoms of pyloric spasm or stenosis, the latter must be looked on as the more likely pathologic condition.

In most of our cases in addition to the spasm of the pylorus, we have encountered a spasm of the cardia. That this functional disturbance has not been met with frequently by others can be accounted for only by a difference in technic. If a catheter is forcibly pushed down the esophagus into the stomach, a moderate increase of resistance of the cardiac sphincter will readily be overcome, and just as readily escape observation. However, if the catheter is inserted slowly and gently, it will be noted that there is frequently a definite resistance persistently met with at a point which is about 15 or 16 cm. from the lips, whenever we attempt to enter the stomach. When a very soft rubber tube, such as the duodenal ball-tube, is employed, we find this obstruction intensified, so that, as in the two tests in Case 1, it becomes impossible to pass the cardia unless we relax this sphincter by having the baby swallow some liquid (accessory method). This interesting syndrome of pylorospasm adds weight to the argument of those who favor a neuropathic origin for this condition. In the case of an infant 7 weeks of age suffering from pylorospasm, it was found that frequently the food did not even enter the stomach, but was checked at the cardia and quickly regurgitated. In this case it was impossible to pass the soft tube into the stomach. When the catheter was inserted into the stomach this organ was found to be absolutely empty, a condition which in my experience is very exceptional.

Another observation which is interesting, and which has not, to my knowledge, been previously described, is an anomaly of secretion in the duodenum frequently accompanying pylorospasm. For some time it has been realized that many cases of spasm of the pylorus are accompanied by a marked increase in secretion of gastric juice. In the two cases which I have detailed, this was true. In addition there was an increase in the secretion of the duodenal fluid. In the first case in Test 3, the first one in which I was able to enter the duodenum, 8 c.c. of fluid was aspirated within twenty-five minutes; in the next test 6 c.c. was obtained in thirty minutes, and in the seventh test, the only other in which the juice was

collected, 8 c.c. of alkaline fluid was secreted in one hour. Comparative tests on other infants show unequivocally that this far exceeds the normal total of secretion for such short periods. The second case gives evidence that this hypersecretion, or "duodenal succorhea," as it may be termed, may persist even when the spasm is not present. It will be seen that in the first test of Case 2, which, it will be remembered, was undertaken when the baby was no longer vomiting, although gavage had been necessary about three weeks previously, a marked duodenal hypersecretion was noted; 13 c.c. of alkaline, greenish juice being obtained in thirty minutes. The fluids in all these instances were examined for the three pancreatic ferments, and found to contain them rather in excess, so that we must conclude that in cases of pylorospasm accompanied by gastric hypersecretion there is often also a pancreatic hypersecretion. It is well established that the gastric juice serves to stimulate the pancreatic juice, but tempting as this explanation appears, it may be that both secretions have a common exciting cause.

I have intimated that some cases of pylorospasm are not accompanied by gastric hypersecretion. Most observers now distinguish between these two groups of cases. The case of the 7-weeks-old infant whom I referred to in connection with the obstinate cardiospasm, well illustrates this distinction. There was only one test performed, and this showed the stomach absolutely free of hydrochloric acid both at the beginning and at the end of the test. In this instance there was likewise a hypersecretion of duodenal fluid, instead of the succorhea which we encountered in the previous cases, so that using also the pancreatic secretion as a criterion we can differentiate two groups of cases.

#### USE OF THE CATHETER FOR THERAPY

In infants persistent vomiting may result in extreme inanition, or even death. We see this most frequently, perhaps, in cases of pyloric stenosis or of pylorospasm. In spite of all our efforts to relieve the spasm or to provide an appropriate food the vomiting persists. But in addition to this group of cases there are others less sharply defined, termed by some merely "persistent vomiting," for want of a more exact term, in which the infant dies of inanition, and the stomach is found normal at autopsy. Gittings<sup>3</sup> recently reported three such cases. Again, during or shortly following the acute period of some of the infectious diseases, such as pneumonia, vomiting may supervene and threaten or end the life of the weakened infant. I believe cases of this description are more frequent than is generally realized.

The main treatment of vomiting in infants, whatever its cause, may be summarized as dietetic, the selection of an appropriate food, or as mechanical, which includes the washing of the stomach, as well as feeding

3. Gittings, J. C.: Arch. Pediat., August, 1911, p. 661.

by means of the tube directly into the stomach. But even these methods are not always successful, and many infants succumb to marasmus or finally to some secondary infection. It is in these extreme instances in which the ordinary measures fail, that I believe duodenal feeding has a place. The two radiographs (Figs. 3 and 4) which I have had reproduced clearly demonstrate that this procedure is feasible. They show us the catheter in the duodenum, and the bismuth-milk mixture in the various coils of the intestine. Figure 3 shows this particularly well. In adults Einhorn has employed duodenal feeding. For the purpose of feeding, the catheter is introduced in the usual way, and is inserted to about the 40 cm. mark, if this can be accomplished without force. When the catheter has entered this distance, I have refrained from moving it in and out, in order not to irritate the intestine. For the same reason, as well as on other physiologic grounds, I have always had the milk heated to about 100 F. It is probably also of advantage, judging from experiments *in vitro*, to have the milk peptonized, although I have many times given raw milk in this way without observing signs or symptoms of indigestion. The infant must be fed slowly. In some cases this precaution is forced on us, as the fluid enters the intestine with difficulty, and it even becomes necessary to force it onward by means of pressure, which is most readily carried out with the aid of the aspirating bulb. But where the fluid has a tendency to run rapidly through the funnel, which is attached to the catheter, the flow should be obstructed, and ten to twenty minutes should be consumed for the entire feeding. Otherwise we run the risk of inciting antiperistalsis by overdistending the gut, and of causing regurgitation of the fluid from the intestines into the stomach. Indeed this happens to an inconsiderable extent whenever we introduce large quantities of liquid directly into the intestine. We may then find that some of it, perhaps an ounce, has found its way back to the stomach, and may later be regurgitated, although the bulk of the food has been satisfactorily retained.

I have had an opportunity of feeding a considerable number of infants by this method. In most cases I have done so but once or twice, because further opportunity did not present itself. In these instances the report has been that the food was entirely or almost entirely retained. Two urgent cases in which "duodenal gavage" was continued for some days seem worthy of a detailed report:

CASE 3.—B. B. was admitted September 6 to Beth Israel Hospital, suffering from lobar pneumonia. The child was 10½ months of age, had been ill five days, and gave a history of cough, dyspnea and fever. By September 11 the temperature was normal, falling by lysis. On September 7 the infant began to vomit its feeding, which consisted of 6 ounces of milk, 2 ounces of barley water, and 4 per cent. sugar every four hours. The vomiting increased in frequency, until by September 13 the child was retaining very little nourishment. Smaller quantities of food were given, lavage followed by gavage, sodium citrate, small doses

of codein before feedings, but all to little purpose, and the child sank into a very critical condition. Accompanying a rapid loss of weight, the temperature dropped and remained subnormal (Figs. 5 and 6). On the morning of September 15, I introduced 4 ounces of milk mixture (three-quarters milk, one-quarter barley, sugar 2 per cent) into the duodenum and it was retained. The day following I repeated this procedure with favorable result, so that regular duodenal feedings every four hours were begun. This was discontinued after four days when it was found that the infant, in addition to having gained in weight, was able to retain most of its food when given directly by mouth. The child did not vomit frequently after this date, and was discharged cured November 14. The feeding was carried out as above described.

This case showed the importance of introducing the food slowly, as whenever it was allowed to stream rapidly through the catheter, marked

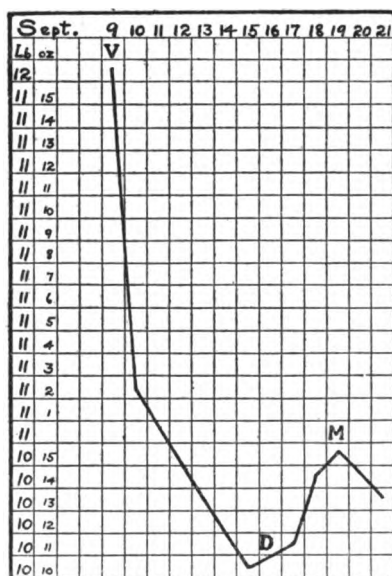


Fig. 5.—Chart showing marked loss of weight in Case 3 during period of vomiting, with gain in weight as the result of duodenal feeding. V, vomiting; D, duodenal feeding; M, feeding by mouth.

gagging would result with a regurgitation of some of the milk. In fact even if the procedure is performed with care there may be a reflux of a small quantity of milk into the stomach. For this reason it is better to limit the amount of feeding to from 1 to 4 ounces according to the size of the child, and the ease with which the milk can be successfully introduced. This is advisable also because these infants are generally suffering from a marked grade of inanition, and it is, therefore, unwise to allow them suddenly large quantities of food.

A second case in which the vomiting was more violent and the inanition more extreme is the following:

CASE 4.—L. N., 18 months old, was admitted to Beth Israel Hospital, September 13, on account of enteritis. The intestinal disturbance yielded to "Eiweissmilch," and all seemed well, when on September 27 the child began to vomit and to give signs of nephritis. By September 29 the child had lost  $1\frac{3}{4}$  pounds, its tongue was dry, its expression anxious; leukocyte count 21,000. Lavage was carried out, and small doses of codein given before feedings. By the day following, it had lost 11 ounces more, that is, almost  $2\frac{1}{2}$  pounds in four days. Lavage had proved of very temporary value. The next day's weighing showed a loss of 2 ounces more (Fig. 7). The child's condition was very serious, its eyes were sunken, its tongue dry, acetone was present in the urine, and all food was rejected whether given by spoon or by tube. The vomiting was markedly projectile in type; when the child lay on its back the milk was ejected in a vertical column of about 3 inches. Food in small quantity, and in weak dilution was resorted to, but all was rejected, even small quantities of water.

October 1 duodenal feeding was attempted on two occasions with success, and the day following four feedings were given in this manner, and one feeding of 1 ounce by spoon. The duodenal feedings consisted of 6 ounces of equal parts of milk and water, with 3 per cent. sugar. This quantity, as I now realize, was unnecessarily large, and generally 1 to 2 ounces were rejected. The 1 ounce feeding by spoon was not retained. October 3, although the child had not gained, it looked better; by the next day it was found to have gained 2 ounces; and by

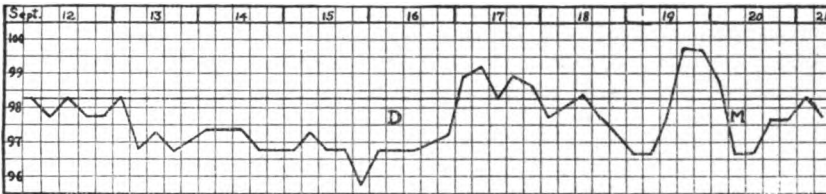


Fig. 6.—Chart showing subnormal temperature in Case 3 during period of vomiting, with rise of temperature as the result of duodenal feeding. D, duodenal feeding begun; M, mouth feeding.

October 6 an additional 6 ounces. The child looked much better, the urine no longer contained acetone, the pylorus seemed relaxed, so that feeding by spoon was once more attempted. The child now retained small quantities of food, and duodenal gavage was entirely abandoned. It was discharged cured from the hospital November 16.

The nature of this sudden attack of vomiting is obscure, but this is not of great moment from the viewpoint of the question of feeding. It was certainly spastic in nature, as proved both by the typically projectile character of the vomiting, and by the resistance which the pylorus offered to the catheter. This resistance became noticeably less after the first few introductions of the tube. It is difficult to judge at present whether this was the result of a dilatation and relaxation due to the instrumentation. It is possible that the passing of the catheter reduced the spasm of the pylorus. This seemed to be true in this instance, as well as in Case 2, described above, in reference to the diagnosis of spasm, and in cases observed by others following the passage of the catheter.

I cannot but feel that the tide was turned in the life of this infant by means of duodenal feeding. There was a sudden change for the better, and although some of the food was regurgitated, as the quantity given was too large, the child gained in weight and strength. It should also be noted that we were able in a few days to abandon feeding by the catheter for regular feedings with the spoon.

It gives me pleasure to acknowledge my indebtedness to Dr. Caillé, and to Dr. Chapin of the Post Graduate Hospital, for the privilege

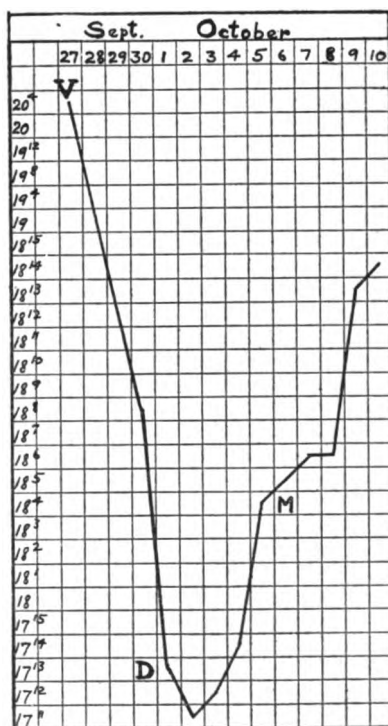


Fig. 7.—Duodenal feeding. Showing loss of weight in Case 4, due to vomiting, and gain following feeding through duodenal catheter. V, period of vomiting; D, beginning of duodenal feeding; M, beginning of mouth feeding.

accorded me of carrying out a large part of this work in their wards, and of thanking Miss Gertrude Fisher for her able assistance.

#### SUMMARY

In infants it is possible without difficulty to insert a soft rubber Nélaton catheter (No. 15 F.), past the pyloric sphincter and into the duodenum. The catheter is introduced in the same way as the ordinary stomach-tube, and, after some experience is acquired, the technic employed becomes almost as simple.



In principle the catheter differs from the duodenal tube previously described by the author mainly in that this instrument does not depend on gravity or peristalsis to direct it to the pylorus. The mere force of inserting it propels it along the natural path of the food to the pyloric opening. This fact not only enables it to be introduced readily and surely, but gives to it the additional advantage of a probe, a pyloric probe with which we may test the tonicity and irritability of this sphincter. Radiographs show that the catheter invariably, on entering the stomach, bends sharply to the left to reach the fundus, and that therefore the more vertical position of the stomach of the infant, does not account for the ease with which the duodenum is entered.

It is probable that unknowingly others have entered the intestine by this method, and that in many instances reports as to the contents or the capacity of the stomach in infancy have been subjected to this source of error.

By means of the catheter we can readily diagnose pylorospasm, and differentiate it from vomiting due to other causes. In the case of spasm we meet with a persistent resistance encountered at the same point whenever we attempt to advance the catheter; this is frequently accompanied by irritability of the pylorus. The spasm may be felt to relax suddenly and enable us to enter the intestine.

Marked pyloric stenosis can be diagnosed from the failure to transgress the pylorus after repeated attempts. A mild degree of stenosis, so slight as to allow of the passage of the catheter, cannot be differentiated from simple spasm.

Cardiospasm frequently accompanies pylorospasm. This sign has been frequently overlooked, due to the too forcible insertion of the stomach tube. If a soft rubber tube, such as was originally used, is introduced into the esophagus, it may be found even impossible to enter the stomach. Frequently as the result of this spasm the food does not enter the stomach, being checked at the cardia.

Just as a marked gastric secretion frequently is associated with pylorospasm, so also is an increased duodenal secretion (duodenal succorhea). This secretion is found to contain protease, lipase and amylase to a marked degree, so that in this connection we may speak of a pancreatic hypersecretion or succorrhea.

There are cases of cardiospasm and pylorospasm unaccompanied by increased gastric secretion. In a case of this kind there was likewise no pancreatic hypersecretion.

The catheter is of value in the therapy of pylorospasm. Its passage through the pylorus seems to relax the ring and in this way to diminish the vomiting. It would seem of advantage to test this method of dilating the pylorus, and to pass the catheter frequently in such cases.

Another form of therapy consists of duodenal feeding. Radiographs show that this is feasible. It should be reserved for such cases as do not retain food given by gavage, and the food should be given slowly and in not too large amounts. In cases of this kind it has been found of great value.

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## A STUDY OF THE CEREBROSPINAL FLUID AND BLOOD IN ACUTE POLIOMYELITIS \*

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### THE CEREBROSPINAL FLUID

There are two ways in which a careful study of the cerebrospinal fluid in acute poliomyelitis may help to throw light on the disease. On the one hand, the changes observed may facilitate early diagnosis and thus enhance the value of any method of treatment which may be discovered in the future, and on the other hand, the variations in the character of the fluid, as observed during the progress of the disease in each case, may give some information as to the usual course of the process and thus be an aid in determining how far any given remedy is effective or to what extent the natural course of the disease may be influenced. The following study was thus made with the twofold object of determining whether the examination of the spinal fluid may be an aid in early diagnosis, and what changes occur in the fluid during the course of the disease.

Previous investigations along this line have not been very extensive. Most writers report only a few cases, and those who have apparently made a large number of lumbar punctures have not submitted the fluids to very careful examination. The results obtained are somewhat variable, but in general the fluid is said to contain an abnormal amount of albumin and a sediment consisting of lymphocytes, large mononuclear cells and occasionally polymorphonuclear cells. Important work has been done by Gay and Lucas,<sup>1</sup> whose contributions are the most valuable in this field. Their studies have embraced the spinal fluids from monkeys in the incubation period, the prodromal stage and the acute stage, and from eleven human cases in the preparalytic stage. Besides noting the character of the cells, the number of cells per cubic millimeter has been estimated. In the eleven early cases the cell count varied from fifty-five to 580 per cubic millimeter and the percentages of mononuclears from seventy-five to 100. Chemical examinations were omitted. Sophian<sup>2</sup> reports that the globulin test is positive in the early stages.

\*This paper will form part of a monograph on the clinical aspects of acute poliomyelitis to be published by the Rockefeller Institute for Medical Research.

\*From the Hospital of the Rockefeller Institute for Medical Research, New York.

1. Gay and Lucas: *Arch. Int. Med.*, 1910, vi, 330; Lucas: *AM. JOUR. DIS. CHILD.*, 1911, i, 230.

2. Sophian: *Arch. Pediat.*, March, 1911.

Inasmuch as previous work by Wollstein,<sup>3</sup> Römer and Joseph,<sup>4</sup> and Gay and Lucas<sup>1</sup> failed to demonstrate the presence of any specific antibody in the spinal fluid in acute poliomyelitis, we have confined our study to simple chemical and cytological examinations.

It has been our object to see the cases as early as possible after the onset of the disease, to make a lumbar puncture on admission to the hospital, to repeat the puncture every two to four days in the early stages, and in the later stages to make a puncture every five to ten days while the case was under observation, or until the fluid became normal. We have examined in all 233 fluids from sixty-nine cases. The number of cases seen in the first week of the disease (dating from onset of symptoms, not of paralysis), was forty-three, in the second week forty-five, in the third week forty, and in the fourth week thirty. The number of cases seen later in the course was much smaller. It is to be regretted that the number of preparalytic and abortive cases was so small — of the former, four, and of the latter, only two were seen in the active stage. It was, however, rare that cases were referred to the hospital until a positive diagnosis, based on the appearance of paralysis, had been made by the attending physician.

The methods used for the examination of the cerebrospinal fluid have included estimation of the pressure, determination of the number of cells per cubic millimeter and the types of cells present, estimation of the chlorids and observation of the power of reducing Fehling's solution, and on the presence of globulin. Globulin was tested for by the butyric-acid method of Noguchi and the relative strength of the reaction noted. Thus "very slightly plus" (v. s. +) indicates a faint precipitate, which is, however, definitely more than that obtained with normal spinal fluids; "slightly plus" (s. +) is the term applied to reactions giving a well-marked cloud or a slightly flocculent precipitate; "plus" (+) signifies a precipitate coming down in large flocculi; and "double plus" (+ +) a heavy flocculent precipitate. The reaction was performed with accurately measured amounts of spinal fluid and of reagents, and the reading made after five to ten minutes' standing.<sup>5</sup> The gross appearance of the fluids was very constant. Almost all were clear, colorless and watery. A few, only, showed the slightest opalescence. On standing, a delicate web-like clot formed in a small proportion of cases. Clot formation was most frequently seen in the early stages of the disease. It bore no apparent relation to the globulin content of the fluid.

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3. Wollstein: *Jour. Exper. Med.*, 1908, x, 476.

4. Römer and Joseph: *München. med. Wehnschr.*, 1910, lvii, 568.

5. To 0.2 c.c. spinal fluid is added 0.5 c.c. butyric acid solution (10 per cent. butyric acid in 0.85 per cent. solution of sodium chlorid). The mixture is boiled, 0.1 c.c. normal sodium hydrate solution added, and then boiled again.

The results obtained by several of these methods may be dismissed briefly. Pressure determinations were made in a number of cases and the readings were usually above normal. The pressure was read in millimeters of spinal fluid in a tube of 1.0 mm. bore. No extremely high readings were obtained, and in some instances normal pressures were seen during the early stages of the disease. On the whole, the estimations of pressure were unsatisfactory, as the patients were usually crying children.

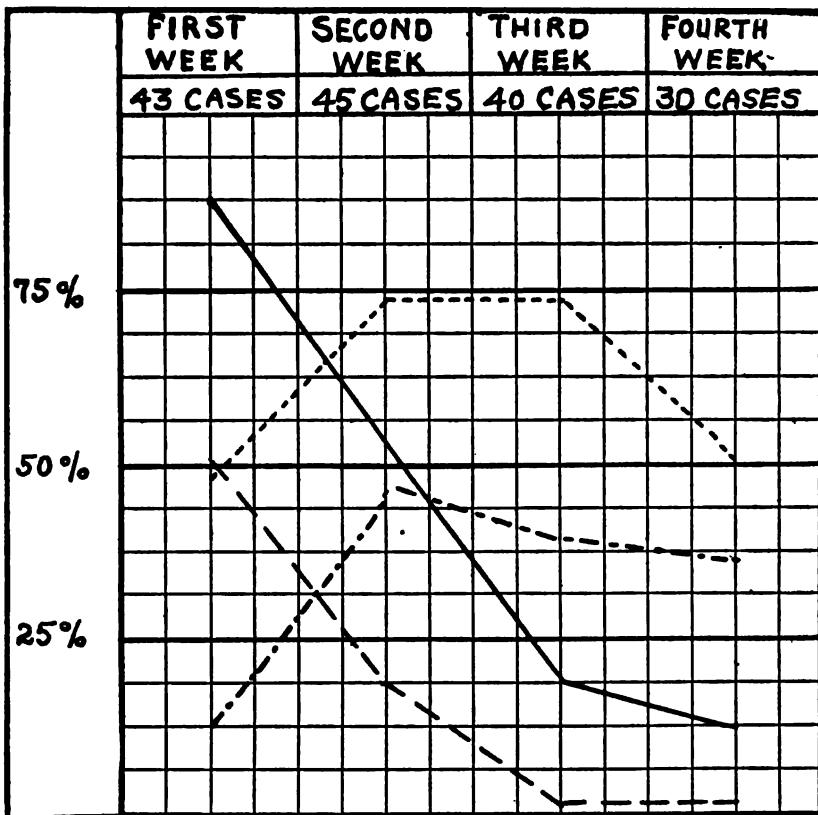


Chart showing variations in cell-count and in globulin content of cerebrospinal fluid in infantile paralysis. ——— Percentage of cases with cell-count above normal. — — — Percentage of cases with cell-count above 50 per c.mm. . . . . Percentage of cases with globulin "s+ ". —.—.— Percentage of cases with globulin "+" or over.

The chlorids were estimated in a series of cases with the idea that they might throw light on the inorganic substances in the fluid. No marked deviations from the normal were observed. Every fluid examined showed a power of reducing Fehling's solution which was, roughly speaking, normal. This reaction serves as a point of differentiation from many

fluids in cases of meningitis, in which the reducing substance may be absent.

The type of cell present in the fluid was almost always the mononuclear. A large number of differential counts showed that the relative number of the different types of mononuclear cells was of comparatively little importance, so in later observations we were content with merely noting the relative number of mononuclear and polymorphonuclear cells. In several instances, numbers of very large phagocytic cells containing vacuoles and broken-down cells were seen. Once this occurred several weeks after the onset of the disease, in association with a sudden rise in the cell count resembling that seen in acute meningitis. Polymorphonuclear cells, except in small number and probably depending for the most part on a slight admixture of blood, were, except in a very few instances, absent after the first week of the disease. Early in the disease, however, and in the preparalytic period, the polymorphonuclears sometimes outnumbered the mononuclears and made up 80 to 90 per cent. of the total.

The results described by Flexner and Lewis<sup>6</sup> of a study of the cerebrospinal fluid of a monkey after inoculation with the virus of poliomyelitis are interesting. Twenty-four hours after inoculation the fluid contained "a considerable number of small cells, hardly exceeding a lymphocyte in size but showing a polyform nucleus, a few lymphocytes and some red corpuscles. At the expiration of forty-eight hours, the white cells have increased in numbers, but the cells with polyform nuclei still predominate. At the expiration of seventy-two hours, a large number of mononuclear cells have appeared and the fluid presents a striking opalescent appearance. On the day of paralysis the fluid tends to be only slightly cloudy and contains a mixture of large and smaller (lymphoid) mononuclear cells and a few cells with polymorphous nuclei." Lucas, too, found in the monkey during the prodromal stage "a marked increase in the cells, often reaching 1,000 per cubic millimeter. In this stage, also, polymorphonuclears are still present, in some cases as high as 60 per cent., though the large mononuclears and lymphocytes were very evident. In the early acute stage the increase in cells is very marked. The cells are now, however, mostly of the lymphocytic or very early form of cells, and sometimes very hard to place, as they are apparently undifferentiated cells." Of his eleven preparalytic human cases, however, only one showed less than 87 per cent. mononuclears, and that had 75 per cent. mononuclears. A return of polymorphonuclears later in the disease, as was reported by Lucas as occurring in monkeys, was not noticeable in our human cases.

The cell count was made immediately after the fluid was obtained. The first portion of fluid obtained was used, but controls made by com-

6. Flexner and Lewis: Jour. Am. Med. Assn., 1910, liv, 1140.

paring counts of early and late portions of the fluid showed no important discrepancy. While the normal number of cells per cubic millimeter of spinal fluid is usually given as three to five, we have considered the upper normal limit as ten to twelve. In general it may be said that the highest cell counts are found in the early days of the disease, and that there is a progressive falling off as time advances. Thus of forty-three cases in the first week, twenty-three showed fluids with over fifty cells per cubic millimeter and thirty-eight with cell counts above normal. Two cases showed in the prodromal period 990 and 650 cells, respectively. Of forty-five cases in the second week, in eight the counts were over fifty, and in twenty-three cases they were above normal; of forty cases in the third week, in only one was the count over fifty, and only in eight above normal. On the other hand, six cases in the first week, twenty-two cases in the second week and thirty-two of the forty cases in the third week showed normal counts.

In contrast to the cell count which thus tends to be high in the early part of the disease, the globulin content is usually low in the first part of the acute stage, especially as compared with the cell count. It rises during the second and third weeks and then gradually falls, though frequently globulin is present long after all acute symptoms have passed (see chart). We have seen a strong (+) globulin reaction on the forty-sixth day of the disease. During the first week, only six of forty-three cases showed at any time a globulin reaction of + (see above) or more. During the second week twenty out of forty-five showed a + reaction, in the third week sixteen out of forty, and in the fourth week nine of thirty cases. On the other hand, sixteen cases in the first week showed an absolutely normal globulin reaction. Five cases in the second week and only three in the third week were negative for globulin. Most cases, even on discharge, gave a globulin reaction which varied from slightly to markedly above the normal. In eleven cases the fluids were followed until both cell count and globulin reaction became normal. The return to normal occurred in the third week in two cases, in the fourth in two cases, in the fifth in one case, in the sixth in two cases, in the seventh in three cases, and in the tenth week in one case.

Of the sixty-nine cases studied, only two never showed any abnormal fluids. In each of these cases the fluid was examined but once, on the twenty-fifth and thirty-third days of the disease, respectively. One case showed, in five fluids taken between the ninth and forty-first days of the disease, no evidence of abnormality other than the slightest positive globulin reaction (v. s. +), and another, in three fluids obtained on the ninth, sixteenth and twenty-third days, gave similar results. Four cases, including one abortive case, showed fluids which, except for the slightest

globulin reaction, were normal at the first tapping and subsequently became more definitely positive.

The commonest type of fluid seen in the whole series is one with normal or slightly increased cell count and a well-marked globulin reaction. There are, however, two other distinct types of fluid met with. The one is a fluid with a high cell count and a normal or very slight globulin reaction, and the other is a fluid with a normal or low cell count and a very marked globulin reaction. Twenty-six cases showed at some time a globulin of not over s. + and cell count of fifty or over. Twenty of these occurred in the first week, and in twelve the count was over 100 cells per cubic millimeter. On the other hand, sixty-two fluids from thirty-four cases gave a globulin reaction of + or more. In thirty-three of these the cell count was normal and in fifty-five it was not above forty per cubic millimeter. That the two types of fluid are fairly distinct is shown by the fact that only five cases showed fluids with both a high cell count (over fifty), and even a moderately high globulin. Each type of fluid is, moreover, quite definitely characteristic of a stage in the disease. The cellular exudate is almost always associated with the earliest days of the acute stage, the albuminous exudate with the latter part of the acute stage. It is interesting that of ten cases seen within the first three days after the onset of symptoms, all but one had a cell count of over fifty (one was thirty-seven), and six were over 100. On the other hand, six gave a negative globulin reaction. In four the reaction was s. +.

#### DIAGNOSIS

As regards early diagnosis, the cases examined before the onset of paralysis are of the greatest interest. Six cases were seen in what may be termed the prodromal period. Four of these developed paralysis later and two proved to be of the abortive type. In one case a single lumbar puncture was made on the fourth day after the onset. The fluid gave a cell count of 650 per cubic millimeter, 90 per cent. polynuclears, and a + globulin reaction. Three days later the child suddenly developed paralysis and in five hours died of respiratory failure. A second case, the sister of a child already in the hospital, was seen on the day after the onset of symptoms. The spinal fluid contained 990 cells per cubic millimeter, 90 per cent. of which were polymorphonuclears, and the globulin reaction was s. +. On the following day one leg was paralyzed and the cell count of the spinal fluid was 627 per cubic millimeter with 80 per cent. mononuclears. The next day both legs were paralyzed and the cell count was 1,221 per cubic millimeter, with 92 per cent. mononuclears including many large phagocytic cells. The globulin reaction was +. Thus two cases seen very early in the course of the disease showed fluids with unusually high cell counts, and with a marked pre-



dominance of polymorphonuclear cells. In one of them the change of the cell picture from the polynuclear type to the mononuclear type could be followed coincident with the onset of the paralysis. Three other cases in the prodromal period, one an abortive case and two becoming paralyzed on the day of the first lumbar puncture, gave cell counts of thirty-seven, ninety-four and 113 per cubic millimeter, with 100 per cent., 93 per cent. and 83 per cent. of mononuclear cells, respectively, and globulin reactions which fell within normal limits. Finally in one abortive case lumbar puncture on the second day after the onset of symptoms gave a wholly normal fluid. On the third day the cell count was sixty-two per cubic millimeter, with 89 per cent. mononuclears and a s. + globulin reaction. On the sixth day the cell count was fifty-nine per cubic millimeter, all mononuclears, and globulin s. +. On the eleventh day the spinal fluid was again normal. That this was in fact an abortive case of poliomyelitis was proved later by showing that the patient's blood-serum was capable of neutralizing active virus when mixed with it and injected intracranially into a monkey.

In these six cases, then, examination of the spinal fluid gave evidence which was helpful in making a diagnosis of poliomyelitis before the onset of paralysis. Similar evidence was afforded by eleven cases of Lucas and by one of Frissell.<sup>7</sup> In none of these twelve cases, however, was a large percentage of polynuclear cells found. But it seems of importance to call attention to the fact that a fluid whose cytology resembles that found in cerebrospinal meningitis and other types of purulent meningitis may also occur in the early stages of poliomyelitis.

The question arises as to whether there is any relation between the situation and extent of the paralysis or the severity of the disease and the character of the spinal fluid. Conclusions on this point cannot be drawn from the number of cases seen by us. It would seem, however, that in cases in which the paralysis is limited to arms or to cranial nerves, the lumbar puncture fluid is rather apt to show less deviation from the normal than where the legs are involved. This is, however, far from being a constant finding. Several cases which had acute symptoms (pain, irritability), lasting for an unusually prolonged period, gave an unusually large and persistent globulin reaction. Moreover, the disappearance of the acute symptoms was frequently coincident with a diminution in the globulin in the spinal fluid. The fatal cases showed nothing in the fluid on which to base a bad prognosis.

Since the infecting organism in poliomyelitis is too small to admit of its being seen, even if it is present in the cerebrospinal fluid, and since the more complicated biological tests have failed to prove the presence of antibody in the fluid, the diagnostic value of examinations of the

7. Frissell: Jour. Am. Med. Assn., 1911, lvi, 661.

spinal fluid by simple chemical and microscopic methods must necessarily be merely relative. While in cerebrospinal meningitis, in tuberculous meningitis, in pneumococcus, influenzal and similar types of meningitis one obtains specific information and is usually enabled to make a positive diagnosis from an examination of the spinal fluid, the value of the examination in poliomyelitis is necessarily less direct. Thus in a fluid containing a high percentage of polymorphonuclear cells, the failure to find any organisms would certainly be suggestive of poliomyelitis. The difficulty of differential diagnosis is perhaps greater when one has a fluid with a lymphocytic cytology. Lucas has discussed at length the non-specificity of the cytological findings in various meningeal conditions, and finds a similar cell picture in encephalitis, poliomyelitis, meningismus, tuberculous meningitis and syphilis of the central nervous system. Because, however, the examination of the spinal fluid in poliomyelitis lacks specific value, it would be very wrong to conclude that it was not an important aid in diagnosis, or that lumbar puncture should not be performed in suspicious cases. Routine blood examinations and the usual urinary analyses have comparatively rarely any specific diagnostic value. Their greatest usefulness consists, perhaps, in helping to rule out certain possibilities, and in focusing one's attention on a narrower group of processes. Within such a group the blood or urine examination, partly of itself, and partly when brought into line with clinical experience, may, by bringing either negative or positive evidence, be the determining factor which inclines one toward the correct diagnosis. The value of positive findings in spinal fluid examinations is undoubted. The value of negative results in examination approaches it in importance. Thus in the case of poliomyelitis, the failure to demonstrate specific changes in the spinal fluid should rule out several serious meningeal conditions, the differential diagnosis of which from poliomyelitis in the preparalytic stage may be most confusing. On the other hand, by the demonstration of non-specific changes (for we have seen that by far the greater number of fluids in poliomyelitis are in one way or another abnormal), a host of other conditions which may simulate incipient poliomyelitis are removed from further consideration. Among the small group of remaining possibilities, certain characteristic types of fluid, as for instance one with a high cell count and a normal globulin reaction, may be of some value in deciding the diagnosis. More careful studies of the fluids in conditions other than poliomyelitis may throw further light on the differential value of non-specific fluids. At any rate, when even the non-specific fluid of poliomyelitis is considered in association with the clinical features of the case in hand, the diagnosis can probably be made in the great majority of cases even in the preparalytic stage. The ease and safety with which lumbar puncture can be performed and

the simplicity of the examination of spinal fluids should make the method one of much wider use than it is at present. The value of any future method of treatment of poliomyelitis must depend eventually on the possibility of early diagnosis, for where nerve cells have been destroyed, the results from any therapeutic measures will be comparatively small.

#### CONCLUSIONS

The spinal fluid from cases of acute poliomyelitis during the first few weeks after the onset of symptoms shows, in the great majority of instances, deviations from the normal.

Fluids taken during the early days of the disease, and especially before the onset of paralysis, tend to show an increased cell count with a low or normal globulin content.

At this early stage the polymorphonuclear cells may amount to 90 per cent. of the total. Most fluids, however, show lymphocytes and large mononuclear cells almost exclusively.

After the first two weeks the cell count usually drops to normal, or nearly to normal, and there is frequently an increase in the globulin content. A slight increase in globulin may persist for seven weeks or more.

Analogous changes may be found in the spinal fluid of abortive cases. All fluids examined reduced Fehling's solution.

The examination of the cerebrospinal fluid in acute poliomyelitis, while giving, as far as is yet known, no specific diagnostic criteria, is of the utmost value as an aid to diagnosis both in preparalytic and in abortive cases.

#### THE BLOOD

The complete symptomatology of diseases caused by filterable virus in man is not yet established. Certain clinical features of the two most studied examples, hydrophobia and poliomyelitis, have been well described, but the blood picture which has been so thoroughly determined in most infectious diseases and is of such value in differential diagnosis, is little discussed. Owing to the resemblance of numerous features of rabies and poliomyelitis, it seemed that a comparative study of the blood changes in the two diseases might throw some further light on the nature of the human body's reaction to invasion by infecting agents of this type. The large systems of medicine make no mention of blood counts in either malady. In one exhaustive report of thirty cases of rabies by Brain and Maloney the blood of one patient is reported to have had a "slight polymorphonuclear leukocytosis."

Through the courtesy of the attending physicians at the Presbyterian Hospital, in New York, the following blood counts from cases of hydrophobia are available:

Patient 1.—Male, aged 35; temperature, 99.3 F.; W. B. C., 9,400; polymorphonuclears, 76.0 per cent.; lymphocytes, 10.5 per cent.; large mononuclears, 9.8 per cent.; transitionals, 3.8 per cent.; basophils, 0.0 per cent.; eosinophils, 0.0 per cent.

Patient 2.—Male, aged 27; temperature, 100 to 103 F.; W. B. C., 13,000: Polymorphonuclears, 76.5 per cent.; lymphocytes, 11.0 per cent.; large mononuclears, 10.0 per cent.; transitionals, 2.5 per cent.; basophils, 0.0 per cent.; eosinophils, 0.0 per cent.

Patient 3.—Male, aged 27; temperature, 103 F. (Nov. 26). W. B. C., 34,450: Polymorphonuclears, 85.0 per cent.; lymphocytes, 12.0; large mononuclears, 0.0 per cent.; transitionals, 0.3 per cent.; basophils, 0.0 per cent.; eosinophils, 0.0 per cent.

Patient 3.—Temperature 103 F. (Nov. 27). W. B. C., 30,200: Polymorphonuclears, 87.0 per cent.; lymphocytes, 10.5 per cent.; large mononuclears, 0.5 per cent.; transitionals, 2.0 per cent.; basophils, 0.0 per cent.; eosinophils, 0.0 per cent.

Obviously, except in the first case, in which the total count was normal, there was a leukocytosis. In all the cases a definite polynucleosis existed with low lymphocyte percentage.

In the literature of poliomyelitis there are conflicting statements about the leukocyte count. LaFetra<sup>8</sup> in New York and Müller<sup>9</sup> in Germany have made the most extensive observations on the blood. The former reported in six cases a leukocytosis, running from 13,400 to 20,600. He says nothing about the differential counts. Müller, on the other hand, reporting fifteen cases, says that a leukopenia of from 3,000 to 5,000 was always present in the acute stage. He gives no figures but states that there was a slight increase of the lymphocytes. Gay and Lucas<sup>10</sup> made a comparative study of the blood in monkeys suffering from the experimentally produced disease and in children with poliomyelitis. In monkeys they report a leukopenia during the acute stage with a lymphocytosis ranging from 10 to 20 per cent. above normal. The protocols of the human cases, however, do not offer very convincing support to their statements that a similar blood picture occurs in the human cases. The lowest count reported from a 9 months' baby (Case 2), is 7,800 to 12,200. The other three cases showed the following leukocyte counts:

Case 1, 20 months, 11,600 to 17,400.

Case 3, 2 years, 12,000.

Case 4, 5 years, 13,400.

These blood counts can hardly be considered below normal. In two of their four cases a lymphocytosis, "slight" for one and "62 per cent." for the other, is given. Of the other two cases, one, a child of 5 years, had a normal differential count and the other a polynucleosis of 75.5 per cent.

The accompanying tables and ensuing statements are based on the study of the blood of our seventy-one hospital patients. The actual figures given represent the counts from only fifty-nine cases. The records

8. La Fetra: Arch. Pediat., 1909, xxvi, 328.

9. Müller: Die Spinale Kinderlähmung, Berlin, 1910.

10. Gay and Lucas: Arch. Int. Med., 1910, vi, 330.

of the other twelve cases were omitted because those patients suffered from other conditions which might have affected the blood count. Care was taken to avoid collecting the blood at times when a digestive leukocytosis might have been present. The total white count was made in the usual way, the blood and 0.5 acetic acid being mixed in a 1-10 pipette and the drop counted on a 0.1 mm. cell. For differential counts Wright's modification of the Romanowski stain was used.

TABLE 1.—DIFFERENTIAL BLOOD-COUNT IN CASES OF ACUTE POLIOMYELITIS

Age, Years	Number of Cases		First Week							
				Poly.	Lymph.	L.Mono.	Trans.	Baso.	Eosin.	Stim.*
½-1	4	23,900-35,600	Max.	59.0	57.0	18.0	15.0	0.5	1.0	1.5
			Min.	25.0	16.5	1.0	0.5	0.0	0.0	0.0
			Aver.	42.0	36.7	9.5	7.7	....	....	....
1-2	12	12,200-26,000	Max.	70.0	50.0	13.5	13.5	1.0	15.5	1.0
			Min.	26.5	16.5	1.5	2.5	0.0	0.0	0.0
			Aver.	48.2	33.2	7.5	8.0	....	....	....
2-3	5	9,000-23,000	Max.	64.5	43.0	14.0	18.0	1.5	7.0	1.5
			Min.	32.5	20.0	1.5	3.0	0.0	0.0	0.0
			Aver.	48.5	31.5	7.7	10.5	....	....	....
3-4	4	6,900-15,000	Max.	72.0	29.0	8.5	13.0	0.5	9.0	1.0
			Min.	55.0	17.0	1.0	1.5	0.0	0.0	0.0
			Aver.	68.5	23.0	4.7	7.2	....	....	....
4-5	6	12,400-33,000	Max.	81.0	37.5	26.5	14.5	1.5	0.0	0.5
			Min.	44.5	18.6	2.6	4.5	0.0	0.0	0.0
			Aver.	62.7	28.0	14.5	9.5	....	....	....
5-7	4	8,800-23,300	Max.	77.0	24.0	11.7	5.5	1.0	8.0	1.0
			Min.	62.2	16.7	0.5	1.0	0.0	0.0	0.0
			Aver.	69.6	20.3	6.5	3.2	....	....	....
8-21	3	12,000-16,700	Max.	75.0	17.5	17.0	9.5	0.05	1.5	0.0
	—		Min.	59.0	13.0	0.5	4.5	0.0	0.0	0.0
	38		Aver.	67.0	15.2	8.7	7.0	....	....	....
Second Week.										
1-2	11	12,300-30,400	Max.	73.0	56.0	23.0	11.0	6.0	5.5	0.05
			Min.	37.0	9.0	0.5	4.0	0.0	0.0	0.0
			Aver.	55.0	32.5	11.7	7.7	....	....	....
2-3	8	9,800-20,000	Max.	61.5	41.0	23.5	10.5	5.0	7.5	0.5
			Min.	38.0	10.0	2.0	2.0	0.0	0.0	0.0
			Aver.	49.7	25.5	12.7	6.2	....	....	....
3-4	2	14,600-19,700	Max.	84.0	21.5	13.5	6.5	0.0	0.5	0.5
			Min.	57.5	6.5	6.5	3.0	0.0	0.0	0.0
			Aver.	70.7	14.0	10.0	4.7	....	....	....
4-5	1	28,000								
5-7	1	11,800		76.5	14.5	4.5	3.5	0.0	0.5	0.5
8-12	1	12,000		62.0	17.5	16.0	3.5	0.0	1.0	0.0
			24							

\*Stim—"Stimulation Forms" of Türk.

			<i>Third Week</i>							
Age, Years	Number of Cases			Poly.	Lymph.	L.Mono.	Trans.	Baso.	Eosin.	Stim.
1-2	13	8,300-26,100	Max.	67.0	58.5	7.5	13.5	1.5	10.5	1.0
			Min.	30.5	22.0	0.0	0.5	0.0	0.0	0.0
			Aver.	48.7	40.2	3.7	7.0	....	....	....
2-3	5	12,800-23,700	Max.	63.5	42.5	24.5	9.5	0.5	3.0	0.5
			Min.	45.0	16.0	0.0	2.5	0.0	1.0	0.0
			Aver.	54.7	29.2	12.2	6.0	....	....	....
3-4	2	10,300-15,700	Max.	59.5	37.5	6.5	14.0	1.0	6.5	0.0
			Min.	45.0	20.0	2.0	5.5	0.0	0.5	0.0
			Aver.	52.2	28.7	4.2	9.7	....	....	....
4-5	1	28,000								
5-7	1	28,000		72.0	9.0	2.0	10.0	0.0	2.0	0.0
8-12	2	7,800-18,000	Max.	67.5	28.0	4.5	9.0	0.0	2.5	0.0
			Min.	63.0	19.5	3.5	2.0	0.0	1.0	0.0
			Aver.	65.2	23.7	4.0	....	....	....	....
	24									
			<i>Fourth Week</i>							
1-2	11	10,100-24,700	Max.	60.0	63.5	41.0	17.0	1.0	4.0	2.5
			Min.	26.5	21.5	35.0	1.5	0.0	0.0	0.0
			Aver.	43.2	42.5	23.7	9.5	....	....	....
2-3	5	14,600-23,600	Max.	65.0	46.0	10.5	10.0	0.5	6.0	0.0
			Min.	26.5	23.5	0.5	4.5	0.0	0.0	0.0
			Aver.	45.7	34.7	5.5	7.2	....	....	....
3-4	2	11,000-19,800	Max.	51.0	46.5	1.5	8.5	0.5	8.0	0.5
			Min.	40.5	37.5	0.0	3.5	0.0	2.0	0.0
			Aver.	45.7	42.0	0.7	6.0	....	....	....
4-5	3	10,500-22,300	Max.	58.5	33.8	10.5	4.0	0.6	2.7	0.3
			Min.	42.0	27.9	6.4	2.0	0.0	0.5	0.0
			Aver.	50.2	30.8	8.4	3.0	....	....	....
5-7	2	14,200-21,000	Max.	64.5	36.0	12.5	2.5	0.5	0.0	0.0
			Min.	49.5	25.0	7.5	1.5	0.0	0.0	0.0
			Aver.	57.0	30.0	10.0	2.0	....	....	....
8-12	2	9,400-10,700	Max.	64.5	26.0	2.5	8.0	0.5	4.5	0.5
			Min.	62.5	....	0.0	4.5	0.0	0.5	0.0
			Aver.	63.5	....	1.7	6.2	....	....	....
	25									
			<i>Fifth Week</i>							
1-2	6	9,100-23,600	Max.	60.5	56.0	13.5	10.0	0.5	6.5	1.0
			Min.	38.0	20.5	1.0	2.0	0.0	1.5	0.0
			Aver.	49.2	38.2	7.2	6.0	....	....	....
2-3	6	15,000-27,000	Max.	58.0	44.5	9.5	14.0	0.0	9.5	0.5
			Min.	40.0	21.5	0.0	5.0	0.0	3.5	0.0
			Aver.	49.0	33.0	4.2	9.5	....	....	....
3-4	3	12,800-16,700	Max.	60.5	30.0	10.5	6.5	1.0	4.0	0.5
			Min.	54.5	25.0	6.0	2.5	0.0	2.0	0.0
			Aver.	57.5	27.5	8.2	4.5	....	....	....
4-5	2	6,300-20,000	Max.	85.0	24.0	12.0	7.0	1.0	2.0	1.0
			Min.	62.5	19.0	0.5	3.5	0.0	....	0.0
			Aver.	73.7	21.5	6.2	5.2	....	....	....
	17									

		<i>Sixth Week</i>							
umber			Poly.	Lymph.	L.Mono.	Trans.	Baso.	Eosin.	Stim.
Cases									
3	9,600-26,700	Max.	40.0	69.0	10.0	15.0	0.5	2.5	2.0
		Min.	23.0	32.0	0.0	0.5	0.0	0.5	0.0
		Aver.	31.5	50.5	5.0	7.7	....	....	....
2	10,200-22,800	Max.	57.0	44.0	4.5	9.0	0.5	3.5	2.0
		Min.	45.0	29.0	2.0	0.5	0.0	0.5	0.5
		Aver.	51.0	36.5	3.2	4.7	....	....	....
2	13,100-28,600	Max.	64.0	34.0	8.5	3.0	0.0	1.0	0.0
		Min.	57.5	23.5	7.0	1.5	0.0	0.0	0.0
		Aver.	60.7	28.7	7.7	2.2	....	....	....
1	15,000		50.0	32.5	4.0	11.0	0.0	1.5	1.0
1	9,400		47.0	37.5	5.5	4.0	0.0	3.5	2.5
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		<i>Seventh Week</i>							
2	23,700-26,700	Max.	51.0	45.0	10.0	5.0	2.0	6.5	0.5
		Min.	31.5	34.5	9.5	4.0	0.0	0.5	0.0
		Aver.	41.2	39.7	9.7	....	....	....	....
3	15,800-22,300	Max.	70.9	43.6	11.0	7.5	0.5	5.0	0.0
		Min.	42.5	16.0	0.5	3.5	0.0	1.0	0.0
		Aver.	56.2	29.8	5.7	5.5	....	....	....
1	9,800		49.0	30.5	4.0	11.5	0.5	4.0	0.0
2	11,000-12,400	Max.	62.0	54.5	10.5	4.0	9.5	1.0	0.5
		Min.	39.5	16.0	0.5	0.5	0.5	0.5	....
		Aver.	50.7	35.2	5.5	2.2	....	....	....
1	16,000		59.5	22.0	7.5	8.5	0.5	2.0	0.0
<hr/> 9									

		<i>Eighth Week</i>							
2	10,700-12,000	Max.	52.5	37.5	9.0	5.5	0.0	1.5	0.0
		Min.	47.0	35.5	8.5	2.5	0.0	0.5	....
		Aver.	49.7	36.5	8.7	4.0	....	....	....
1	16,000		58.0	32.5	2.0	6.0	0.0	2.0	0.5
<hr/> 3									

		<i>Tenth Week</i>							
1	10,800		61.5	23.5	4.5	9.0	0.0	0.0	0.5

		<i>Twelfth Week</i>							
1	16,000		54.0	38.0	5.5	2.0	0.0	1.5	0.0

The first set of tables is designed to show minimal, maximal and average counts for groups of cases. A second, composite table shows minimal, maximal and average total leukocyte counts of all ages together by weeks. Such a compilation seems justifiable because the age variation is much less in respect to the total than the differential leukocyte count.

TABLE 2.—COMPOSITE TABLE SHOWING MINIMAL, MAXIMAL AND AVERAGE TOTAL LEUKOCYTE COUNTS OF ALL AGES BY WEEKS

Week	Number of Cases	Maximal	Minimal	Average
First	38	24,600	12,200	18,400
Second	24	24,500	12,000	18,250
Third	24	23,300	10,400	16,800
Fourth	25	20,300	11,800	15,900
Fifth	17	21,800	10,800	16,300
Sixth	9	23,200	10,500	16,800
Seventh	9	19,500	15,000	17,250
Eighth	3	14,000	10,700	12,400
Tenth	1	.....	.....	10,800
Twelfth	1	.....	.....	16,000

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TABLE 3.—THIS TABLE COMPRISES SEPARATELY THE COUNTS FROM PREPARALYTIC AND ABORTIVE CASES

Case	Age, Yrs.		W. B. C.	Poly.	Lymph.	L.Mono.	Trans.	Baso.	Eosin.	Stim.
B. X.	5		15,000	....	....	....	....	....	....	....
		3/0*	7,000	81.0	....	....	....	....	....	....
J. S.	2½	2/0	14,200	58.5	31.5	7.0	3.0	0.0	0.0	0.0
C. T.	¾	2/0	35,600	32.0	55.0	1.0	9.0	0.0	1.0	1.5
E. N.	6	6/0	23,200	76.0	17.0	3.0	2.5	0.0	1.0	0.5
H. B.	6	2/0	8,800	77.0	17.5	0.5	4.0	0.0	0.0	1.0
		3/0	11,200	79.5	14.5	0.5	4.5	0.0	0.5	0.5
		6/0	5,600	68.5	22.0	1.5	6.0	0.0	1.0	1.0
		13/0	11,800	76.5	14.5	4.5	3.5	0.0	0.5	0.5
P. T.	2	1/0	15,000	52.5	31.5	13.5	1.5	0.5	0.5	0.0

\*The numerator of the fraction signifies the day of the disease, the denominator the day of the paralysis.

It is obvious from these figures that while in most cases in the preparalytic stage the total leukocyte count varies within the normal, there is a tendency toward the upper limits. More cases showed counts well above than below the usual extremes. In the differential counts there is a definite polynucleosis with the one exception of an 8 months' infant in whom the relation of polymorphonuclears and lymphocytes is normal. Furthermore, the lymphocyte percentages in all the other cases are distinctly below the usual figure.



TABLE 4.—DIFFERENTIAL COUNTS IN NORMAL INDIVIDUALS

Age, Years		Poly.	Lymph.	L.Mono.	Eosin.	Baso.
$\frac{1}{2}$ -1	Max.	33.9	58.5	12.2	4.5	0.8
	Min.	24.6	50.5	7.3	0.0	0.1
	Aver.	30.4	55.9	9.6	2.6	0.4
1-2	Max.	39.7	58.8	11.7	6.0	0.5
	Min.	27.5	45.3	6.7	1.6	0.0
	Aver.	36.3	51.2	8.5	3.2	0.2
2-3	Max.	44.3	55.0	11.3	6.0	1.2
	Min.	33.2	43.5	5.0	0.5	0.0
	Aver.	38.7	49.0	8.2	3.1	0.4
3-4	Max.	54.1	47.6	16.2	4.2	0.9
	Min.	36.2	32.2	5.0	1.5	0.0
	Aver.	44.7	39.1	11.2	2.8	0.5
4-5	Max.	51.7	49.5	6.7	4.0	0.6
	Min.	42.2	38.4	3.4	1.6	0.3
	Aver.	48.5	42.1	6.0	2.6	0.3
5-6	Max.	61.8	36.7	16.0	4.7	1.0
	Min.	52.6	21.2	6.5	0.7	0.3
	Aver.	56.5	29.9	10.0	2.5	0.6
6-7	Max.	61.3	34.1	15.7	4.7	0.6
	Min.	52.3	24.5	8.1	0.1	0.0
	Aver.	56.0	30.4	10.8	2.2	0.2
7-8	Max.	72.0	39.1	15.2	3.5	0.2
	Min.	45.2	21.1	6.7	0.0	0.0
	Aver.	54.4	32.5	11.6	0.1	0.06

In one instance in which blood counts were made by the physician before the patient came to the hospital, a low total count appeared, 7,000 two days before the paralysis and 3,000 on the day after paralysis. The differential count, however, showed a polymorphonuclear increase each time (81 per cent. and 58 per cent). Except for this one case which subsequently became one of our seventy-one, we have not seen a true leukopenia. One abortive case in a little girl 6 years of age showed counts of 5,600 to 11,800. In the youngest children the leukocyte counts have been highest, and the polymorphonuclear increase has been both relatively and actually more marked than in the older patients. A glance at the tables, however, will show that all ages have a high white cell count. Furthermore, the leukocytosis persists for a surprising length of time. In nine cases, for example, observed during the seventh week, the leukocytes numbered 15,000 to 19,500 with an average of 17,250.

The differential count presents a fairly constant picture. For comparison, a table of differential counts from normal individuals prepared

by Schloss<sup>11</sup> is printed. There is obviously in poliomyelitis an increase in polymorphonuclear cells of 10 to 15 per cent. above the normal. This increase appears irrespective of the patient's age, though the youngest children have shown perhaps the highest polynuclear counts. Contrary to the observations of Müller and Gay and Lucas, we have found a diminution of lymphocytes. In general, they have been from 15 to 20 per cent. below the normal percentages. Notwithstanding, however, the great variation which these cells present in relation to age, the finding of low lymphocyte percentages has been constant in all our cases of poliomyelitis.

No abnormality was noted in the number of transitional and large mononuclear cells. In a good many cases there has been an increase in eosinophils. This finding, however, has not been sufficiently constant to justify further comment. No counts were made of the red cells, nor were any hemoglobin estimations recorded. There has been nothing, however, in the appearance of the patients to suggest an anemia resulting from the disease; nor did the stained erythrocytes look abnormal. No actual counts were made of blood platelets, but the impression was gained in the course of many differential counts that these elements were somewhat increased.

To sum up, then, we have found in the blood of patients with poliomyelitis a constant and marked leukocytosis. In several instances the count has been as high as 30,000. In only one case has there been a definite leukopenia. Besides the increase in total cells, there has been an equally constant increase of polymorphonuclears of 10 to 15 per cent. above the normal, and a diminution of lymphocytes of 15 to 20 per cent. The other forms of leukocytes have shown no abnormalities.

What the significance of this leukocytosis, and especially the polynucleosis, may be, is at present not clear. In view of the fact that the brunt of the body's attempt at defense falls on the lymphatic system, and that the cells which are marshalled at the point of attack seem to be lymphocytes, one might be led at first thought to expect a lymphocytosis in the blood. On the other hand, it is conceivable that the lymphocytes are relatively few in the circulation because they are constantly being withdrawn to meet the invasion of the virus in the spinal cord. It will require, however, a more fundamental knowledge of the kind of reaction the body develops to this type of infecting agent before a correct explanation of the blood picture can be made. At all events, while the blood picture in poliomyelitis is perhaps not any more specific than are the changes in the spinal fluid, it is at least helpful. If taken in connection with other available evidence, a leukocytosis of 15,000 to 30,000 is

11. Schloss: "The Normal Percentages of the Different Varieties of Leukocytes in Infants and Children," *Arch. Int. Med.*, 1910, vi, 638.

distinctly suggestive of the disease in question, especially if the polymorphonuclear cells are increased at the expense of the lymphocytes.

NOTE.—Since this paper has reached the proof, certain additions to our knowledge of the pathology of poliomyelitis have appeared which indicate definitely the general systemic nature of the infection. In view of the finding in many viscera of areas of focal necrosis with many polynuclear phagocytes, an explanation for the polymorphonuclear cytolysis in the blood is at once suggested. Furthermore, the appearance of many disintegrating lymphocytes lends support to the idea that rapid destruction of lymphocytes underlies the lymphopenia. Both these explanations for the blood picture are offered purely as hypotheses.

Sixty-Sixth Street and Avenue A.

## ATROPHY OF INFANTS \*

PROFESSOR AD. CZERNY

STRASSBURG

The term "atrophy of infants" was formerly used to designate a disease *sui generis*. It was characterized clinically by the fact that children, who had developed well up to a certain time, gradually began to fail and eventually died, presenting the picture of a progressive and often extreme grade of emaciation. This peculiar condition, which was seen only in infants, came to be known under different names, such as *tabes mesenterica*, *athrepsia*, *pedatrophy* and "decomposition." But the change in name brought with it no scientific or practical advance. The nutritional disturbances stand out so prominently in the clinical picture of the disease that they generally came to be recognized as the most essential feature. When the children presented a greater or less degree of atrophy, infectious processes were likely to make their appearance in various parts of the body and these hastened the fatal termination of the atrophy.

The pathologic-anatomic findings appeared to justify the assumption that the atrophy was a disease entity. The autopsies showed not only a general emaciation, but it was believed, in addition, that there was an actual atrophy of the intestinal tract. The intestinal musculature appeared to be thinned out to a marked degree and the intestinal glands to be hypotrophic. Therefore it appeared reasonable to believe that as a result of this, the nutrition of the child must have suffered and eventually could not be maintained at a point at which life was possible. More recent investigations have shown, however, that the views that have been held in regard to the atrophy of the intestinal tract are no longer tenable; that the autopsy findings have been misinterpreted, in that what appeared to have been a thinning of the intestinal wall due to atrophy, is in reality a thinning out of the muscular layers due to distention, and the histologic findings in the intestinal mucosa are directly referable to post-mortem changes. An examination of the intestinal mucosa of a child that has died as a result of atrophy shows that it is absolutely normal, provided the examination is made soon after death and with all the necessary precautions. At the present time, therefore, the pathologist can regard this atrophy only as the result of a development, far behind what it should be, and of an extreme emaciation.

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\* Translation by F. C. Zapffe, M.D., Chicago, of a paper read by the author at Strassburg, Nov. 7, 1911.

This unsatisfactory state of our knowledge has led to the laying of altogether too much importance on the secondary infections of atrophic children. This is especially true of otitis media. As a matter of fact, pus is often found in the middle ear of children who have died in a condition of atrophy. A natural result of this finding was the belief that bacterial products of a poisonous kind could be absorbed from the purulent areas produced by these bacteria, and that in consequence the atrophy is nothing more than the result of a septic intoxication. The question was never asked of the clinician whether the otitis media first appeared when the child was already atrophic, or whether it ushered in the entire process. The finding of a purulent otitis media was regarded as sufficient ground for teaching physicians that atrophy is the result of otitis media.

One thing at least can be said for pathologists: they were at all times of one mind. They were at first all fully convinced that there was an intestinal atrophy and they were later convinced that otitis media played a most alarming part in the high infant mortality. This unanimity of opinion was not to be found among the clinicians at any time. There are so many views held as to the nature of atrophy that I cannot, at this time, refer to them all. I will content myself with mentioning those definite facts to which we can hold fast and what outlook these allow for medical activity.

Atrophy is not a disease *per se*, but a disturbance in growth and in general nutrition, which is the result of nutritional disturbances, or of infectious processes, or of both. The clinical picture may be the same in all these instances, but a differentiation based on etiology is of great importance to us on account of prophylaxis and therapy. If the disease is a nutritional disturbance, splendid results can be obtained by dietetic management. If, however, an infection, which we cannot therapeutically influence, is the exciting factor, we are often placed in a position where we can neither check nor cure the atrophy.

Before going deeper into the subject, I should like to put the question before you, whether under like conditions every nursing infant becomes atrophic or whether to do so is the tendency of only certain ones. And I should like to answer this question by saying that the occurrence of atrophy, irrespective of the causes producing it, is distinctly the result of a constitutional anomaly. We are all aware that the same errors are made in feeding many children, and yet only a proportion of these become atrophic. The same difference obtains with children suffering from infectious processes. For instance, a child may pass safely through an attack of whooping-cough, bronchopneumonia or otitis media without any severe influence on his general condition or his growth being apparent, whereas the general condition of other children may be affected

in the severest way by these same diseases. Naturally, in the case of infections one thinks of a different degree of virulence of the organisms. But even when there may be actually a variation in virulence this does not by any manner of means explain the great difference in the effect on the general condition and the growth of the child.

Every clinician, and still better, every family physician, knows that there are many families in which an infant, as the result of a nutritional disturbance or of an infection, will temporarily lose weight, but in which a case of atrophy never develops. While on the other hand, there are families in which even under good conditions, one or more infants pass through some stage of atrophy. These facts are of the very greatest importance, because the majority of physicians have been rather inclined to accept the statement that atrophy is always the result of poor nutrition, deficient care and poor hygiene. Of course, it cannot be denied that all these factors may greatly influence the course of the atrophy; yet everything is not to be explained as a result of them, because we continually see children who do not become atrophic in spite of every improper and dangerous kind of food. If we restrict our studies entirely to the children of the working class, we hardly obtain information as to the fundamental character of atrophy, for in this class it is seldom possible to obtain as exact a history as is necessary to clear up the question or to exclude the non-essentials. However, as I have previously stated, this condition of atrophy in infants is seen not only in children of the lower classes, but also in those better situated, and it is in these that one is able to obtain a more exact idea of the essential process of the disease.

We may differentiate three classes of children that may suffer from this condition more or less during infancy. The first group comprises children that have inherited the exudative diathesis (Exudative Diatheses, Czerny). The milder forms are recognized only by the difficulties in the way of proper nutrition of the child. Children with a more severe form of exudative diathesis readily become atrophic if the diet is not very carefully regulated. It is especially instructive that this condition also occurs in breast-fed infants. The majority of these children may be recognized from the very beginning by the fact that, irrespective of whether they are nursed by their mothers or by wet-nurses, they regain their birth weights late and also that they do not show the development and increase in weight which is characteristic of normal children under similar conditions. If, in severe cases, breast milk is the only food given, on the basis that it is the best food for all children, the complete clinical picture of atrophy may develop. This takes place the more readily because children with the exudative diathesis are susceptible to infections and are hindered in their development by such to a most marked degree. Continued study of this atrophy as a result of an exudative diathesis has convinced me

that its development in the beginning is favored by the injurious effect of improper food. A change from a milk rich in fat to an artificial food containing much carbohydrate and little fat, brings about a cure of the atrophy. If the diet is regulated so that these children do not become too fat or retain too much water, the disposition to infection, which is characteristic of the exudative diathesis, becomes less.

Among the better classes the children receive attention more promptly and medical advice is sought early, so that it is relatively seldom that severe grades of atrophy occur. Among the lower classes the mother usually experiments with the diet for a while herself, or she seeks the advice of other women, especially midwives, whose knowledge for such cases is insufficient, and it is on this account that one can see in children's hospitals and infants' homes a large number of children with exudative diathesis in the atrophic stage. The cases are not thankless for therapeutics; and examples of cure furnish the chief objects of advertisement for children's departments.

The second class or group of children who readily fall victims to atrophy, are those of neuropathic and psychopathic parents. They offer much greater difficulty in the way of treatment and the results under even the most favorable circumstances are often very unsatisfactory. The extreme irritability of the nervous system of the intestinal tract and certain psychic peculiarities furnish the foundation for the atrophy. I should not wish, however, to be misunderstood as maintaining that every child of psychoneuropathic parents must present the same pathologic qualities. Such children inherit sometimes an irritability of one part of the nervous system and sometimes of another, and only one group of children in this class is in danger of becoming atrophic during infancy. The excessive irritability of the intestinal nervous mechanism is manifested in the main by the fact that these children vomit on slight provocation. The vomiting is sometimes so severe that it is almost impossible to administer sufficient food, so long as a fluid diet is necessary. When a soft diet can be given in place of the fluid diet, the vomiting ceases. Sufficient time may have elapsed, however, to have produced an atrophy, the result of insufficient nourishment.

So far as the intestines are concerned, this state of the nervous system shows itself by the fact that such children react to irritation in a way that normal children would not, and have numerous stools, and because numerous, of an abnormal character. As a result of this, we see that even the unavoidable variations in the composition of the mother's milk may produce diarrhea. The result is the same with artificial feeding. These children react with diarrhea to a relatively small amount of carbohydrate in the diet. As a certain amount of carbohydrate in the food is an absolute necessity for the welfare of a child, and especially for a

gain in weight, those who receive the carefully regulated quantity of carbohydrate necessary remain backward in weight and become thereby more or less atrophic. When certain psychic anomalies are present the difficulties of the situation are manifestly increased. The children of neuropathic parents often have the trait of persistently refusing articles with a taste to which normal children readily become accustomed. The difficulty is then that the child so positively refuses the food that we have ordered that he can hardly be made to take it. Unfortunately, instinct does not induce these children to take only such food as is beneficial to them and to refuse that which could be injurious. They often drink greedily a food as a result of which they have plainly become atrophic, and energetically refuse for days the taking of a food by which they eventually will be cured. The treatment of such children always requires a wide experience, and the exercise of great patience and energy. These factors are not always obtainable and therefore it is not astonishing that such children often present severe grades of atrophy even under favorable circumstances.

It should also be mentioned that these psychopathic children are almost always to be recognized by their bad sleeping and great restlessness. They respond to stimuli which the normal child would not notice and often with evidences of dislike. This circumstance increases the danger of atrophy as a result of alimentary causes, because those responsible for children may feel called on, on account of the restlessness, to experiment with the food and do not always do this intelligently and successfully.

From what has been said it is sufficiently apparent that in the case of many children of psychoneuropathic parents, there are numerous factors that may make proper and sufficient feeding difficult or almost impossible. Most of the children seen in clinics and in institutions with whom unsatisfactory results are obtained, belong to this class. And still it is not infrequently possible with proper care to keep them alive. A study of the death-rate of infants shows that this type contributes largely to the mortality. This is not solely the result of the difficulties mentioned but because in such children there are still other anomalies of innervation and these have very bad results especially if they affect the circulation.

In the third class or group are the children with the "hydropic" constitution who in consequence of disturbances of nutrition readily develop atrophy. Children with such a tendency show differences in salt and water retention from normal children. These children retain readily large quantities of water in their tissues. However, the bond between the water and the salts, the carbohydrates and the colloidal substances in the tissues must be much weaker than under normal conditions because



the slightest nutritional disturbance causes wide variations in the water content of the body. This is shown, even when no disturbances are present, by the great variations in the daily body weight. Children of this group will readily gain a great deal of weight when a diet rich in sugars and salt is given. Acute nutritional disturbances and infectious diseases cause such an extreme loss of fluid as to lead to an atrophy which is recovered from with difficulty.

It is quite evident from what has been said, that atrophy may result from many different causes. In the one instance, a child with exudative diathesis may become atrophic as the result of a food rich in fat; in another instance, a neuropathic child may reach apparently the same condition in consequence of an insufficient quantity of food, and in the third case, the lability of the water content of the organism is responsible for similar results.

A consideration of the constitution of children makes it clear to us that there are certain prerequisite conditions that must be present in the body in order that atrophy may develop, but this gives us no clear idea as to the pathogenesis of the condition. Atrophy is characterized by a cessation of normal growth in the entire organism. This disturbance in growth manifests itself in one direction by the absence of increase in body weight or even by a loss. This is easily understood because in such cases the development of fat ceases. Emaciation of varying degree is the external evidence of this. The atrophic child does not grow nor does he accumulate fat even when given a food which under normal conditions would lead to an increase in body weight and increase in fat. If one is inclined to the belief that the absence of fat is caused by a lack of development of adipose tissue, one may say that atrophy is a disturbance of growth which is most manifest in the lack of development of adipose tissue.

Both the failure of general growth and of fat formation occasioned by atrophy are, however, fully reparable. As soon as the nutritional disturbance is overcome or the infection ceases, growth proceeds in the normal manner and the delay is compensated for. We must conclude, therefore, that the disturbance is not a deep-seated one in the cell-complex of the infant's organism. The nature of the injury has not been positively ascertained. From comparison with the etiology of disturbances of plant physiology we may assume that inorganic substances play a considerable part in the production of atrophy. I cite, for instance, the striking influence that potassium exerts on the growth of plants. In the acute nutritional disturbances of infants the organism loses, according to published observations, a particularly large amount of potassium. If potassium exerts an effect on animal cells similar to that on plant cells, then the failure of growth in atrophy is understandable. But the condi-

tions are apparently not as simple in the human organism. It would be, at the present time, very presumptuous to ascribe the disturbances of growth in atrophy to the loss of a single mineral substance. But it is in this way possible for us to conceive how apparently dissimilar causes may give a similar clinical picture of atrophy. They all lead to the loss of mineral substances and apparently chiefly of those which are of determining influence for the growth of the cells.

Similar disturbances are also seen in the case of older children and yet in these, the clinical picture of atrophy is not easily produced. As I have mentioned before, infants living under like conditions do not all become atrophic. To explain this difference we must consider the facts which at present are known to govern the growth of the infant and those which govern the growth of the older child. We know that in the case of the former, it is not exclusively the material furnished in the food which is responsible for growth but that certain deposits in the body are drawn on and that these are present at the time of birth and are gradually used up during the lactation period. Under normal conditions these deposits suffice to compensate for a greater or less loss, the result of pathologic processes. In the case of the child who is hereditarily affected so that one or the other of these depots is deficient, even at birth, consequences of many kinds follow any disturbance that may arise, and one of these consequences is atrophy. That this is not a consideration of mere theoretical value is seen from the fact that what theoretically should cure the atrophy, actually does so. It is only with difficulty and in the less severe grades of atrophy that an exclusively milk diet, even of mother's milk, can produce a cure. In the severe cases this is absolutely impossible. Atrophy requires a food in which, in addition to the milk, certain components should be present in order to compensate for the loss that has taken place as a result of disease. The choice of the substances to be added must be made not alone with the idea of compensation, but it must also, in those cases where disturbances of nutrition have been the determining factor, be one which prevents the return of these.

With this idea in mind the numerous therapeutic measures that are employed have come into use, but at the present time they have more empirical than scientifically proved data to recommend them. At the present time only so much can be said in regard to the food components, that it is the fat that must be much restricted in the treatment of atrophy and that the place of this must be taken by carbohydrates.

# PROGRESS IN PEDIATRICS

## RÉSUMÉ OF WORK ON TUBERCULOSIS IN CHILDREN

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### MODE OF INFECTION

1. Potter, P. S.: The Portals of Entry of Tuberculosis in Children. *Pediatrics*, 1911, xxiii, No. 8.
2. Cobbett, L.: Portals of Entry in Tuberculosis. *Brit. Jour. Child. Dis.*, 1911, viii, 415.
3. Whipman, T. R.: The Portals of Infection in Tuberculosis. *Brit. Jour. Child. Dis.*, 1910, vii, 350.
4. Leuenberger, G.: Contribution to Placental and Congenital Tuberculosis. *Beitr. z. Geburtsh. u. Gynäk.*, 1909-10, v.
5. Gergely, E.: Cases of Congenital Tuberculosis. *Zentralb. f. Kinderh.*, 1910, 321.
6. Peisich, K.: Tuberculosis in Nurslings and Children. *Wien med. Wehnschr.*, 1911, Nos. 4-5, 190.
7. Moeller, A.: Hygiene of the Mouth and Pulmonary Tuberculosis. *München. med. Wehnschr.*, 1910, No. 2.
8. Ehrhardt, O.: Tuberculosis of the Mucous Membrane of the Mouth and Lower Jaw, Following Extraction of a Tooth. *Zentralb. f. Kinderh.*, 1911, xvi, No. 5.
9. Mathews, F. S.: Relation of Tonsil to Tubercular Adenitis. *Med. Rec. New York*, 1910, ii, 515.
10. Simon, G.: Adenoid Growths and their Relation to Tuberculosis, *Beitr. z. Klin. d. Tuberk.*, 1911, xix, No. 2.
11. Warden, C. C.: Relation between the Tonsils and Tubercle Bacilli, *California State Jour. Med.*, 1911, p. 249.

P. S. Potter<sup>1</sup> classifies the portals of entry of the tubercle bacilli into the human organism: (1) Prenatal infection. This may occur in three ways: (a) germinal transmission, (b) placental transmission, (c) intra-partum transmission. The possibility of the seed carrying the disease from the father is demonstrated by Freedman, who injected into the vagina of guinea-pigs after coitus a solution containing bacilli and a week later killed the pigs. He found the bacilli lying in the embryonic layer. (2) Infection through the buccal and nasopharyngeal mucous membranes. (3) Infection through the skin. (4) Aerogenic infection. (5) Enterogenic infection.

After a careful perusal of the literature Potter concludes that any part may serve at some time as the portal of entrance of the tubercle bacillus, but in the majority of instances it is the respiratory or alimentary tract.

L. Cobbett<sup>2</sup> believes that infection in phthisis comes chiefly through the mucous membrane of the respiratory tract. He criticizes the theory of Calmette and the Lille school, that it results from ingestion of tubercle bacilli. This conclusion is based on the possibility of producing phthisis by feeding animals tubercle bacilli through a tube; and on experiments of Vansteenberghe and Grysez, who found anthracosis of the lungs after feeding guinea-pigs india ink and carbon. Cobbett believes the anthracosis was the natural anthracosis of the city-bred guinea-pig. He failed to find any trace of anthracosis after feeding india ink to country-bred guinea-pigs.

In feeding experiments with animals there is always the danger that the material may be aspirated into the lungs. Cobbett showed that organisms could reach the lungs from the air, since cultures taken from the lungs post mortem showed all the organisms usually found in the air. Cultures from other organs remained sterile.

G. Leuenberger<sup>4</sup> contributes records of two interesting cases of placental and of congenital tuberculosis. In the first instance the mother died of tuberculous meningitis and miliary tuberculosis. Tubercle bacilli were found in the fetal liver and numerous miliary tubercles in the placenta. Injection of a small piece of the liver and of the heart's blood of the fetus into a guinea-pig gave rise to pulmonary tuberculosis.

In the second instance the mother suffered from a pulmonary tuberculosis. She aborted. Neither the fetus nor placenta showed any tuberculous changes — but tubercle bacilli were found in the intervillous spaces of the placenta.

Guinea-pigs injected with blood from the umbilical vein developed the disease.

From the study of these two cases Leuenberger draws the following conclusions: When the mother suffers from acute miliary tuberculosis, there can develop numerous miliary tubercles in the placenta and from these tubercle bacilli can penetrate the fetal circulation, and it is also true that without tuberculous changes in the placenta or membranes the bacilli can pass from mother to child; that is, during birth there can be sufficient injury to the chorion vessels to allow the bacilli to pass from the intervillous spaces into the fetal circulation. In view of this fact, immediate tying of the cord of the new-born children of tuberculous mothers is advisable.

K. Peisich<sup>6</sup> doubts the possibility of germinative infection. He says placental disease with penetration of the bacilli into the fetus is the usual method of prenatal infection. He also discredits a specific predisposition to tuberculosis, but regards as more probable a congenital feeble resistance which allows acquired infection. The mode of infection in children varies with age. Young babies are usually infected by their attendants,

either by inhalation or ingestion of the bacilli. The result is a severe pulmonary tuberculosis with rapid generalization. In children up to the school age ingestion of a small number of the bacilli is more usual and the consequence is a benign local form of the disease. Older children are infected as are adults, usually by inhalation of the bacilli.

A. Moeller<sup>7</sup> is of the opinion that an individual can become tuberculous from tubercle bacilli lodged in carious teeth and in the ulcers of unclean mouths.

In order to ascertain the frequency in which tubercle bacilli are found in these locations, he examined two sets of children. The first comprised 194 children with diseased lungs; 153 had carious teeth, 182 had ulcerations in the mouth. Tubercle bacilli were found fourteen times in the carious teeth and the pseudotubercle bacilli twenty-three times; in the ulcerated patches tubercle bacilli were found thirty-five times and the pseudotubercle bacilli forty-two times.

The second series comprised fifty-three healthy children. Twenty-six had carious teeth and forty-one foul conditions of the mouth. No tubercle bacilli were found in the teeth, but pseudotubercle bacilli occurred nine times. In the ulcers tubercle bacilli were found six times and pseudobacilli eighteen times.

While admitting that tubercle bacilli gain access more frequently through the tonsil, the writer still lays stress on the importance of these modes of infection.

O. Ehrhardt<sup>8</sup> reports tuberculosis of the mucous membrane of the mouth and the lower jaw following the extraction of a tooth in a 9-year-old girl. The extraction wound did not heal and there developed in the mucous membrane on either side of the alveolar process a row of grayish-yellow nodules (tubercles). The alveolar process was twice its normal thickness and the cervical glands on the corresponding side were enlarged. The author thinks the movement of the alveolar process indicates an infection at the time of extraction, probably through the instruments. He examined twenty cases of carious teeth in children with tuberculosis and only once found an acid-fast bacillus. This was somewhat thicker than the tubercle bacillus, and may have been Petris' milk-bacillus.

F. S. Mathews<sup>9</sup> says that the tonsil is the probable source of infection of cervical lymph-node tuberculosis, though it may come from a tooth, the pharynx or nasopharyngeal adenoids. No tubercle bacilli were found in fifty-seven tonsils removed for various causes. This confirms the views of Hodenpyl, Wright and Judd, who claim that isolated tuberculosis of the tonsil is rare. Tubercle bacilli were found, however, in five tonsils removed from children suffering from tuberculous cervical adenitis.

C. C. Warden,<sup>11</sup> who found tubercle bacilli in five of twelve tonsils removed according to the usual routine, draws the following conclusions:

(1) Tonsils may oftener be the avenue of tuberculous infection in children than was formerly supposed. (2) The observations of Dieulafoy and Latham are confirmed by this study, namely, that hypertrophied tonsils contain tubercle bacilli in the proportion of 1 to 6. (3) It is possible that tubercle bacilli may assume a vegetative or saprophytic existence in the tonsil.

#### BACTERIOLOGY

12. Report of English Royal Commissions of Tuberculosis. *Tuberculosis*, 1911, x, No. 9.

13. Park, W. H., and Krumwiede, C.: Relative Importance of the Bovine and Human Types of Tubercle Bacilli in the Different Forms of Human Tuberculosis. *Jour. Med. Research*, 1910, p. 205.

14. Litterer, W.: Study of Tubercle Bacilli, Cultivated from Nine Consecutive Cases of Primary Tuberculous Cervical Adenitis. *Lancet-Clinic*, 1911, cx, 443.

15. Moore, V. A.: Elimination of Tubercle Bacilli from Infected Cattle. *Jour. Med. Research*, 1911, xxiv, 517.

16. Rothe, F. W.: Tubercular Infection in Children. *Deutsch. med. Wchnschr.*, 1911, No. 8.

17. Abramowski, H.: Contribution to Study of Scrofula. *Ztschr. f. Tuberk.*, 1911, xvii, 488.

18. Eber, A.: Transformation of Human to Bovine Type of Tubercle Bacillus. *Zentralbl. f. Bakt.*, 1911, lix, 193.

19. Howard, W. R.: Relative Importance of the Infection and Transmission of Bovine and Human Tuberculosis to the Public Health. *Texas State Jour. Med.*, 1910-11, vi, 215.

20. Kossel, H.: Relation of Bovine Tuberculosis to Pulmonary Tuberculosis of Man. *Deutsch. Med. Wchnschr.*, 1911, xxxvii, No. 43, 1972.

21. Jessem, F., and Rabinowitch, L.: Presence of Tubercle Bacilli in the Circulating Blood. *Deutsch. med. Wchnschr.*, 1910, xxxvi, No. 24, 1116.

22. Kurashige, T.: Presence of Tubercle Bacilli in the Blood of Tubercular Patients. *Ztschr. f. Tuberk. u. Heilstättenw.*, 1911, xvi, 347.

23. Krause, A.: Bacillemia in Patients not suffering from Miliary Tuberculosis. *Ztschr. f. Tuberk. u. Heilstättenw.*, 1911, xvii, 436.

The following<sup>12</sup> is a summary of the work done by the English Royal Commission of Tuberculosis on the relation between the form of the disease in man and that in animals.

Three groups of tubercle bacilli can be isolated from tuberculous lesions in man. Group I has all the characteristics of the bovine type. Group II of the human type, and Group III has some characteristics of both the others. Human and bovine tubercle bacilli cannot be differentiated morphologically, but they differ in their cultural characteristics and in their power of producing disease in different animals. They can be regarded as different types of the same organism.

Pulmonary tuberculosis is but rarely caused by the bovine type. On the other hand, 50 per cent. of primary lethal abdominal tuberculosis in children is due to the bovine type, and a large per cent. of cervical gland tuberculosis in children is caused by this type also. There can be no doubt that primary abdominal and cervical gland tuberculosis of bovine origin are due to deglutition of tuberculous material and in all probability

this material is milk containing tubercle bacilli. Preventing the ingestion of living tubercle in the milk will, according to the Commission, diminish abdominal and cervical gland tuberculosis among children. The government control of milk and meat must be more widespread in order to prevent the sale of foodstuffs which come from tuberculous animals.

W. H. Park and C. Krumwiede<sup>13</sup> have made a study of human and bovine types of tubercle bacilli in the different forms of human tuberculosis. According to them, tubercle bacilli, isolated from man, fall into two groups, designated as the human and bovine types. These types differ somewhat, especially culturally and in virulence. The groups differ probably because of their residence in different hosts for long periods of time. The evidence of a rapid change of type is incomplete and inconclusive.

The writers collected from the literature records of tuberculosis in which the type of bacillus was identified and compared the findings with those in a group of their own cases. From a study of both these groups they conclude that the incidence of bovine infection is a negligible factor in adults. In children, however, it causes a considerable percentage of cervical adenitis. Further, in young children an appreciable amount of fatal tuberculosis is due to this infection.

William Litterer<sup>14</sup> examined nine consecutive cases of primary tuberculous adenitis to ascertain the type of infecting organism. In five he obtained cultures of the human; in four, of the bovine type. Most valuable for differentiating these types are the reaction curve test in glycerin bouillon and the test of the virulence of the organism to rabbits. (The bovine type is virulent for rabbits, the human is not.) The reaction curves in glycerin bouillon depends on the chemical reaction of this medium, when the bacilli are grown on it. The first change in either instance is the diminution of the amount of acid. In the case of the bovine bacillus, the reaction may become alkaline; in the case of the human type, the neutral point is closely approached and seldom passed.

V. A. Moore<sup>15</sup> has made an extensive study to ascertain the frequency with which tubercle bacilli are eliminated from infected cattle. He found that the milk from cows with tubercular udders contained tubercle bacilli in large numbers, as well as the milk from animals with open pulmonary or intestinal lesions, or lesions of the organs of reproduction, when it becomes contaminated by feces or uterine discharges.

As a rule, the bacilli are not found in the milk from animals in which a careful physical examination discloses no evidence of the disease, although they may give a positive tubercular reaction.

The writer believes that the number of tubercle bacilli in market milk could be greatly reduced and probably eliminated by frequent and thor-

ough physical examinations of dairy cows and the removal of all which show evidence of the disease.

F. W. Rothe<sup>16</sup> performed a number of inoculation experiments on guinea-pigs with pieces of mesenteric and bronchial glands. He wished to ascertain the frequency of bronchial and mesenteric gland tuberculosis in children in Berlin; the mode of infection, and the type of the infecting organism. Glands from 100 children were examined, and twenty-one of the inoculated guinea-pigs developed tuberculosis. From twenty of these the human bacillus was isolated and from one the bovine. From this study Rothe concludes that 20 per cent. of the children in Berlin are infected with tuberculosis; that the preponderance of infection is through the respiratory tract, and that the bovine type of bacillus plays a part secondary to the human type.

A. Ebers<sup>18</sup> believes that in a number of instances he succeeded, by the passage through rabbits and guinea-pigs, in transforming tubercle bacilli obtained from a human source, and having the characteristics of the human type, into bacilli with all the characteristics of the bovine type.

W. R. Howard<sup>19</sup> enumerates the following ways in which human beings can become infected with the bovine tubercle bacillus: (1) By the use of milk from tuberculous cows and its products. (2) By the use of infected meats, improperly cooked or carelessly handled. (3) Through drinking water from wells where tuberculous animals water. (4) Through flies in the immediate proximity of infected herds carrying the infection to unprotected foods.

H. Kossel<sup>20</sup> examined 709 phthisical patients and found the bovine type of bacillus alone probably three times—surely twice; the mixed form once; and the human type 705 times.

These numbers speak for the fact that phthisis is spread from man to man.

F. Jessem and L. Rabinowitch<sup>21</sup> have undertaken a series of researches to verify the findings of various writers that tubercle bacilli occur in the blood not only in the advanced, but also in the early stage of tuberculosis, and they have been able to detect bacilli in the blood, even in patients afflicted in a mild degree. They believe blood examination a very important diagnostic measure, especially when the sputum cannot be obtained.

T. Kurashige<sup>22</sup> was able to demonstrate tubercle bacilli in 100 per cent. of 155 mild and severe cases of pulmonary tuberculosis. The penetration of the bacilli into the blood does not always give rise to miliary tuberculosis. The finding is of diagnostic but not of prognostic value.

A. Krause<sup>23</sup> has not been able to demonstrate tubercle bacilli in the blood as frequently as other observers. He does not think the prognosis of these bacilli carriers absolutely bad.



DIAGNOSIS

24. Feer, E.: Value of Cutaneous and Conjunctival Reactions in Children. *Beitr. z. Klin. d. Tuberk.*, 1910, xviii, 117.
25. Hamman, L., and Wolman, S.: Cutaneous and Conjunctival Tuberculin Tests in the Diagnosis of Pulmonary Tuberculosis. *Arch. Int. Med.*, 1910, No. 6.
26. Pollack, R.: Tuberculosis in Nurslings. *Beitr. z. Klin. d. Tuberk.*, 1911, xix, No. 2.
27. Klose, E.: Cutaneous Bovine Tuberculin Reaction. *Deutsch. Med. Wehnschr.*, 1910, No. 48, p. 2239.
28. Wallenstein, P. S.: Diagnostic Importance of the Cutaneous Tuberculin Reaction. *Berlin klin. Wehnschr.*, 1911, xlviii, No. 10.
29. Engel, St.: Intracutaneous Tuberculin Test. *Deutsch. Med. Wehnschr.*, 1911, xxxvi, No. 37.
30. Herz, R. and Thomsen, O.: The Wassermann and Cutaneous Tuberculin Reactions in Scrofulous Children. *Berlin. klin. Wehnschr.*, 1911, xlviii, No. 6.
31. Pehu, M.: Reliability of the v. Pirquet Cutaneous Tuberculin Test in Young Children. *Lyon méd.*, 1911, cxvii.
32. Radziejewski, A.: The Cutaneous Tuberculin Reaction. *Ztschr. f. Kinderh.*, 1911, ii, No. 6.
33. Sachs, T. B.: Diagnostic Value of Local Tuberculin Reactions. *Jour. Am. Med. Assn.*, Jan. 21, 1911.
34. Rovere, G.: Significance of conjunctival Reaction in Children. *Rev. di clin. pediat.*, 1911, No. 1.
35. Barheim-Karrer: v. Pirquet Reaction in Non-Specific and Specific Hypersensitiveness of the Skin. *Cor. Bl. f. schweiz. Aerzte*, No. 31, 1910.
36. Sorgo, J.: The Sensitiveness of the Skin of Tubercular Individuals to Bacterial Toxins. *Deutsch. med. Wehnschr.*, 1911, xxxvii, No. 22.
37. Tezner, E.: Specificity of the v. Pirquet Reaction. *Monatschr. f. Kinderh.*, 1911, No. 10, p. 181.
38. Rolly, F.: The Cutaneous Reaction Influenced by Bacteria Toxins. *München. med. Wehnschr.*, 1911, lviii, No. 24, p. 1285.
39. Hirschfeld, H.: The White Blood Cells in Tuberculosis of Childhood. *Monatschr. f. Kinderh.*, 1911, No. 10, p. 38.
40. Leopold, J., and Rosenstern, T.: Significance of Tuberculides in the Diagnosis of Tuberculosis in Infants. *Jour. Am. Med. Assn.*, 1910, ii, 1721.
41. Noeggerath, T. C. and Salle, V.: Head's Zones in Early Tuberculosis of Childhood. *Jahrb. f. Kinderh.*, 1911, xxiv, No. 74.
42. Mayerhofer, E., and Neubauer, R.: Meningitis Tuberculosa and Meningitis Serosa. *Ztschr. f. Kinderh.*, 1911, iii, No. 11 (Orig.).

E. Feer<sup>24</sup> studied the v. Pirquet and conjunctival tuberculin tests in children. He vaccinated 2,000; of these, 171 were tuberculous, ninety-seven suspicious and 1,732 free from tuberculosis; 163 of the tuberculous children, sixty-two of those suspicious, and 277 of those free from tuberculosis gave positive reactions.

A positive v. Pirquet reaction is without doubt specific for tuberculosis. Especially valuable is the test during the first three years; after this time a negative result is of more value than a positive one. Care must be taken to distinguish the spurious from the true reactions. Reactions which disappear in twenty-four hours are not specific.

As to the conjunctival reaction, Feer believes it more often indicates an active tuberculosis than the v. Pirquet, but he does not recommend its use, as severe conjunctivitis and phlyctenules often develop.

L. Hamman and S. Wolman<sup>25</sup> have made the conjunctival and v. Pirquet tests in 1,500 patients. They sum up their opinion of the relative importance of the two tests as follows: "As the specificity of the reactions is now well established in the sense that only patients who have at some time been infected by tubercle bacilli can react, the test shows that a large number of healthy people have been so infected, but as the test remains positive, even when the infection has been overcome, the story it tells is of absorbing interest to the clinician only when the patient is still in his infancy. Reactions during the first year or two of life mean that the patient has been only recently attacked and must be strengthened for combat with the invader, but if the test is negative and the child not moribund or suffering from measles, any suspicions of tuberculosis are dispelled.

"The conjunctival test, if only safe solutions are used, is not nearly so sensitive as the cutaneous test. In event of a negative reaction entire reliance must be placed on other methods of investigation."

R. Pollak<sup>26</sup> agrees that a negative cutaneous reaction in nurslings speaks with the greatest possibility against the existence of a tuberculous focus, which, however, cannot absolutely be excluded. If the reaction is negative, the more delicate "stick-reaction" must be employed. According to Hamburger, this reaction is obtained by injecting beneath the skin 0.1 to 1 mg. of tuberculin. It must not be injected later than the second or third day after vaccination or the increased sensitiveness to tuberculin caused by the vaccination may lead to a general reaction. A positive v. Pirquet reaction proves not only the presence of a tuberculous focus, but that the process is an active one, because latent tuberculosis does not exist in nurslings.

E. Klose<sup>27</sup> vaccinated 120 children, suspected of having tuberculosis, with human and bovine tuberculin. Of these, forty did not react to either; the others reacted similarly to both. Klose offers two explanations. Either the antigens of human and bovine tuberculin are identical or there are two kinds of antibodies formed in the body and each reacts with its particular antigen.

The writer believes that from the results obtained by vaccinating with both tuberculins one can decide which should be used as a therapeutic measure.

P. S. Wallenstein<sup>28</sup> believes the more latent the tuberculosis, the stronger must be the concentration of the tuberculin to cause a reaction and that this usually runs a course of a "late reaction." The more the process leans toward an initial active stage, the weaker should the concentration of the tuberculin be; even a one-eighth per cent. solution can cause a reaction. The more manifest the tuberculosis, all the more

concentrated must be the tuberculin, and in very advanced cases the reaction is negative even with 100 per cent. solutions.

St. Engel<sup>29</sup> declares that the intracutaneous tuberculin test has numerous advantages over other tuberculin tests. He uses one drop of a 1/1,000 solution of old tuberculin and if no reaction follows, increases the strength to 1 per cent., 10 per cent., and 100 per cent. In some instances the patients will react to the larger dose and not to the smaller. The subcutaneous test fails with febrile patients and the cutaneous with patients whose susceptibility to tuberculin is reduced, but the intracutaneous method succeeds when these others fail.

G. Rovere<sup>34</sup> repeated the conjunctival test in thirty non-tuberculous children under 2 years of age, to ascertain whether a local "hypersensitiveness" could be obtained. Each child was tested eight to ten times. The results were negative and substantiated the findings of other authors, that local "hypersensitiveness" cannot be produced by repeated instillations of tuberculin into the eye.

Barheim-Karrer,<sup>35</sup> discussing the condition of hypersensitiveness of the skin to the v. Pirquet test, asserts that children suffering from eczema can give a positive reaction, when there is no focus of tuberculosis. A differential diagnosis can be made only by a second vaccination which is negative in eczema and markedly positive in tuberculosis. Cases of hypersensitiveness to the v. Pirquet test, as described by this writer, fall into two groups, the first including those with severe local symptoms; the second, those with general symptoms.

In the first group the papule is especially large, intensely red, with sometimes a vesicle in the center, rarely an ulcer. The lesions last much longer than in ordinary reactions.

In the second group, beside the severe local manifestations, lesions have occurred in other parts of the body, and phlyctenules, conjunctivitis and rhinitis have all been observed. The general eruptions are especially interesting and resemble measles or scarlet fever, as well as urticaria and erythema urticatum. Their incubation stage is not regular; they may appear ten hours or ten days after the vaccination.

J. Sörgo<sup>36</sup> has added a contribution to the question whether the tuberculous infected organism possesses a specific sensitiveness to tuberculin only or to other toxins as well. He vaccinated the same individual with tuberculin, diphtheria, and dysentery toxin. The reaction was marked in all three instances. Sörgo comes to the conclusion that the v. Pirquet test depends on a local sensitiveness of the skin to the toxin. This sensitiveness is increased in the majority of non-cachectic infected individuals for tuberculin and other toxins.

E. Tezner<sup>37</sup> ascertained that all children who gave positive v. Pirquet reactions reacted also with colitoxin. He absolutely denies the specificity

of the v. Pirquet reaction and thinks it depends on the reaction susceptibility to the protein of any or all bacteria with which the organism is infected.

F. Rolly<sup>38</sup> performed a number of experiments to see if irritation of the skin would interfere with the v. Pirquet tuberculin reaction. Also, if other toxins as those of cholera, dysentery, and pyocyaneus would give reactions. He irritated the skin two hours before vaccination with mustard plasters, iodine, naphthol and cantharides, and found that the reactions to tuberculin were then much less marked and often negative.

Of the children vaccinated with the various toxins, 16 per cent. gave positive results. These could not possibly be anaphylactic or specific reactions as the children had never suffered from these diseases. He found also that their cutaneous reactions not only for tubercle, but for the other toxins, became negative during the course of various diseases.

Rolly believes that cutaneous susceptibility follows other laws than that which governs general susceptibility.

Hanna Hirschfeld<sup>39</sup> examined the blood in the various forms of tuberculosis in children to determine the relation of the white blood cells. She found that prognostic favorable cases show a tendency to lymphocytosis, at times to eosinophilia. Unfavorable cases always show absence of eosinophil cells. Tuberculin injections do not modify the picture.

J. L. Leopold and T. Rosenstern<sup>40</sup> believe the skin lesions are an aid in diagnosing tuberculosis in infancy. They especially call attention to the papulonecrotic tuberculids, which consist of slightly raised papules varying in size from a pinhead to a millet seed. At first they are red but later become brownish and show a scale or crust in the center. The lesions may appear on any part of the skin, but the sites of election are the arms, the lower back and the extensor surface of the lower extremities. The authors found them in 40 per cent. of their cases.

T. C. Noeggerath and v. Salle<sup>41</sup> have studied "Head's zones" in early tuberculous lesions of children. Head found that, when a segment of the spinal cord is irritated through disease of any internal organ, irritation is transmitted to the skin area supplied by nerves from that spinal segment. The technic for eliciting Head's zones is simple. The skin is stroked gently with the blunt end of a pin held vertically. The patients tell when there is pain and when not. Now and then the pain is so severe that the muscles twitch.

The writers studied this sign in forty-six children, of whom twenty-four were clinically suspected of tuberculosis. Of these twenty-four, sixteen showed Head's zones of sensibility; in eight they were absent. In twenty children with no lung-findings the sign was absent.

The areas found sensitive were those supplied by nerves from the second, third and fourth dorsal segments and fourth cervical areas, which,

according to Head, suggest disease at the base of the lungs, and of the bronchial glands.

The writers think from their examination that Head's zones in early or incipient tuberculosis have the same significance as in other diseases.

E. Mayerhofer and R. Neubauer<sup>43</sup> think testing the spinal fluid for organic material by the potassium permanganate method is a very important procedure in the diagnosis of tuberculous meningitis. The method was explained in a former contribution of Mayerhofer, as follows: One cubic centimeter of spinal fluid is mixed with 50 c.c. of distilled water; 10 c.c. of a 25 per cent. sulphuric acid is added, and when these are brought to a boil, 10 c.c. of one-tenth normal solution of potassium permanganate. The whole is kept simmering for ten minutes and then 10 c.c. of one-tenth normal solution of oxalic acid is added, which decolorizes the fluid. Then more of the permanganate solution is added drop by drop, until the first drop leaves a distinct rose color. The number of cubic centimeters of the permanganate solution indicates the amount of organic material.

The spinal fluid from 100 cases, mostly of tuberculous meningitis, was tested. A few cases of meningitis of other origin, a few of convulsions in children, and two cases of poliomyelitis were also tested. In all cases of tuberculous meningitis the index for organic matter was very high, from 2 to 30 and even 37.3. Exudates of tuberculous pleurisy and peritonitis gave the same high figures.

From their studies the authors conclude that a tuberculous meningitis cannot exist without a high reducing power of the spinal fluid to potassium permanganate, although not all cases with high reducing power are those of tuberculous meningitis. The reducing power occurs early in the course of the disease and so is a valuable diagnostic aid.

#### SYMPTOMATOLOGY

43. Ranke, K. E.: Diagnosis and Epidemiology of Pulmonary Tuberculosis in Children. *Arch. f. Kinderh.*, 1910, liv, 279.

44. Aviragnet, E. C., and Tixier, L.: Curable Forms of Acute Tuberculosis in Children. *Arch. d. méd. d. enf.*, 1911, xiv, 321.

45. Pollak, R.: Tuberculosis in Nurslings. *Beitr. z. Klin. d. Tuberk.*, 1911, xix, No. 2.

46. Gaujoux, E., and Maillet: Polyvisceral Tuberculosis in a Child. *Ann. d. méd. et chir. inf.*, 1911, xv, No. 9.

47. Huguenin, B.: Tuberculosis of the Bronchial Glands and Lungs in Children. *Cor. Bl. f. schweiz. Aerzte*, 1910.

48. French, H.: Mediastinal Causes of Chronic Cough in Children. *Lancet*, London, 1911, clxxxi, No. 4593, p. 743.

49. Stoll, H.: The Diagnosis of Bronchial Node Tuberculosis. *Amer. Jour. Med. Sc.*, 1911, cxli, 83.

50. Leiner, C. and Spieler, F.: Disseminated Tuberculosis of the Skin in Childhood. *Ergebn. d. inn. Med. u. Kinderh.*, 1911, vii, 59.

51. Lafarcinade, M.: Tuberculous Meningitis in New-Born Infants—the Somnolent Form. *Med. Press and Circ.*, London, April 19, 1911.

52. Archangelsky, W. G.: Possibility of Cure in Tubercular Meningitis. *Jahrb. f. Kinderh.*, 1911, lxxiv, No. 24.

53. Cassel, J.: Clinical Contribution to Tubercular Peritonitis in Children. *Berlin klin. Wehnschr.*, 1911, No. 48, p. 832.

54. Galliot, A.: Tubercular Peritonitis with Syndrome of Appendicitis. *Arch. de méd. de enf.*, 1911, xiv, 529.

55. Bradshaw, J. H.: Tubercular Peritonitis in Children. *Arch. Pediat.*, 1911, xxviii, 284.

56. Vignard, P., and Thèvenot: Tuberculosis of the Testicles in Children. *Ann. d. méd. et chir. inf.*, 1911, xv, No. 18.

57. Cabannes, M.: Tuberculosis of the Conjunctiva. *Rev. intern. de la Tuberc.*, 1911, xix, 443.

58. Milligan, W.: Aural tuberculosis in Children. *Brit. Med. Jour.*, 1910, ii, No. 26, p. 1693.

K. E. Ranke<sup>48</sup> differentiates three forms of pulmonary tuberculosis in children: (1) Phthisis, which is analogous to that in the adult, is relatively rare, and has a more favorable diagnosis. (2) Generalized tuberculosis, which occurs most frequently in the first and second years and has an absolutely bad prognosis. (3) The so-called hilus catarrh. The children affected with this form are anemic, have scrofulous symptoms, give positive tuberculin reaction, and frequently suffer from tracheal and bronchial catarrh. Examination of the lungs shows changing, localized râles in the apices, with eventually exaggerated, weakened or rough breathing, and lessened resonance on percussion.

R. Pollak<sup>45</sup> has made a study of the clinical manifestations of tuberculosis in nurslings, and thinks the primary lesion at this age is a bronchial gland tuberculosis. This primary defect is not usually diagnosed because of its mild character. Pollak mentions, however, that lately Sluka has reported that it can be regularly discovered by means of the Roentgen rays. Clinical symptoms, says Pollak, manifest themselves only when the glands have reached a certain size, and the two cardinal ones are the high-pitched cough, like the bark of a young dog, and an expiratory crow. Next in importance for diagnosing tuberculosis in nurslings are the skin lesions. Besides lichen scrofulosorum, scrofuloderma and erythema induratum, the writer has frequently found the small papulosquamous tuberculid.

Tuberculous meningitis occurs early in the course of tuberculosis in nurslings. The author found that instances of this rarely gave a history pointing to a primary bronchial gland tuberculosis; that it was discovered post mortem but gave no clinical signs.

Pollak also mentions a latent form of tuberculosis in nurslings. He says that tuberculosis should be suspected in infants properly fed, who, without symptoms on the part of the digestive system, have a stationary weight-curve, or one which runs downward. The only evidence in these children is the positive cutaneous test and the presence of skin tuberculids.

Tuberculosis in nurslings, according to this author, has not so bad

a prognosis as was formerly supposed. The patients frequently survive the first year. The prognosis depends on the source of infection. Infants infected from a virulent source usually develop a severe form of the disease; those infected from a chronic phthisis, or mild form, suffer from a milder curable type. Children who are infected during the first year and survive, develop a typical habitus. They are pale and thin, with flabby muscles. They have long eye-lashes and hair on the temples and between the shoulder blades. The writer has watched this habitus develop in children infected during the first year of their life.

B. Huguenin<sup>47</sup> is of the opinion that the bronchial glands can become infected without any lesion of the lungs. This can take place in two ways, either from a descending or ascending gland tuberculosis or by taking up the bacilli from the intact mucous membrane of the respiratory tract. In the mildest cases the enlarged glands cannot be detected by physical examination. The disease runs the course of a subfebrile or febrile bronchitis, with anemia and emaciation. There are no lung findings and no bacilli in the sputum. The lesion in the glands either becomes encapsulated, caseated or calcified; that is, there is a relative cure, or it progresses and ruptures into a vein with a resulting miliary tuberculosis. The author also describes a hilus tuberculosis resulting from the rupture of the gland into a small bronchus. If the gland becomes secondarily infected with any of the pus organisms, it suppurates and may rupture into the esophagus, pericardium or pleura.

H. French<sup>48</sup> believes that enlarged tuberculous lymph-nodes situated at the bifurcation of the trachea are a cause of chronic cough among children. The right bronchial node is the one most frequently affected and any enlargement of this directly irritates the phrenic nerve and causes paroxysms of coughing. In a number of cases it is possible to demonstrate the enlargement by means of the Roentgen rays. It is important to recognize this as a cause of chronic coughs, so that the general hygienic measures to correct tuberculous infections may be instituted.

H. Stoll<sup>49</sup> thinks it surprising that the diagnosis of bronchial node tuberculosis has not received more attention. To ascertain the reliability of a number of signs regarded as indicative of this condition, he has studied 175 children and compared the results of his examination with the skin tuberculin test.

On inspection the most important sign to be seen is the dilated veins over the anterior aspect of the thorax. On palpation tenderness over the manubrium and sternocostal junction is suggestive, but these tender areas appear less frequently than tenderness over the spines of the upper thoracic vertebræ. Dulness obtained by percussion over the upper part of the sternum has little diagnostic value but interscapular or vertebral

dulness is of decided value, as well as vertebral bronchophony. This is elicited by placing the bell of the stethoscope directly over the vertebræ and having the patient whisper slowly the words, "three-thirty-three." Normally, the tracheal character of the respiratory murmur ceases at the seventh cervical vertebra, but, when enlarged bronchial nodes are present, it is continued downward over the thoracic spines.

The *x*-rays are very valuable in diagnosis. The writer has been able to compare the physical findings with the *x*-ray plate in fifty instances. Calcified nodes are recognized by their sharp, clear shadow, while cheesy ones give a shadow of less density and less clearly marked boundaries. The earliest evidence of the bronchial nodes seems to be a shadow which extends from the anterior tip of the third rib on the right side upward to the first rib. This shadow extends to the right of the vertebræ for a variable distance. A chain of nodes can often be seen along the right border of the heart. The ones about the trachea give a more diffuse shadow than those at the hilus. Quite commonly an enlarged node is observed close to a bronchus.

C. Leiner and F. Spieler<sup>60</sup> describe the various forms of disseminated tuberculosis of the skin in children.

*Lupus Vulgaris Disseminatus*.—The eruption of this form is characterized by nodules from the size of a pinhead to that of a pea, bright red, bluish or brownish in color, and sharply defined from the surrounding tissue. They are of soft consistency and in the early stage of the disease the skin is drawn taut over the upper surface. The eruption is explosive and over night the entire body can be covered with small nodules or they may appear in crops. The lesions may remain unchanged for months or may at any time disappear, leaving behind slightly pigmented superficial scars. Or, by the apposition of new nodules large plaques may form. They do not, however, lead to destruction of the underlying tissues.

*Gommes Scrofulenses Disséminées*.—The primary efflorescences are nodules which develop in the subcutaneous or cutaneous tissues, without any inflammatory reaction. They are hard at first, then soften, and break through the thin bluish-red overlying skin. It takes weeks or months for the thin fluid with cheesy masses to discharge; then scarification sets in, with the formation of bluish-red or bluish scars.

This form frequently appears at the end of the first year of life, and is the first manifestation of a latent tuberculosis.

*Lichen Scrofulosorum*.—The lesions consist of pinhead to needle-sized papules, located around the hair follicles. They resemble lesion of lichen planus.

The papulonecrotic tuberculid is the best-known of all the tuberculids. The primary lesion is a small brownish or bluish nodule which soon becomes grayish white, and indented in the center. A few drops of



creamy pus are exuded and the lesion is covered with a dry crust or scale. As the center dries, the lesion flattens, loses its nodular character finally, loses its crust, and completely heals, leaving behind a characteristic scar, with central depression and a peripheral area of pigmentation.

*Erythema Induratum* resembles erythema multiforme and must be differentiated from this disease. The large, hard nodes, of livid red or violet fading into the normal skin, are usually situated on the lower extremities. They differ from those of erythema multiforme in not being painful or itching. They usually occur in young girls with a scrofulous diathesis.

*Disseminated Miliary Tuberculosis of the Skin.*—This eruption scattered over trunk and extremities has a purpuric character. The single lesions are pinhead to lentil sized, livid red or reddish brown, and do not completely disappear on pressure. The center is sometimes depressed and covered with a crust or scale. As the lesions disappear, they leave behind an indented pigmented spot. This form is a manifestation of a general miliary tuberculosis.

The prognosis of the disseminated tuberculids is not necessarily unfavorable. Even the miliary tuberculids may heal before the inevitable death of the patient. Their diagnostic value is great, for they are often the first manifestations of the disease.

M. Lafarcinade<sup>51</sup> describes a "somnolent" form of tuberculous meningitis, which occurs in young infants. Its onset is gradual; for the first four or five days the child shows a tendency to sleep more than usual, and this becomes more noticeable, until he awakens only to nurse and immediately falls asleep again. Ultimately the sleep is continuous and the child becomes comatose; the eyes remain open. Emaciation is progressive from the beginning. If the pulse is examined several times a day, it is found to vary from hour to hour, perhaps 90 one hour, then 140 to 160. There may be diarrhea and vomiting.

After two weeks of these symptoms the picture is as follows: The child lies in his cradle, usually on his back, with no expression on the face, with the eyes half closed; he cannot be roused; the pulse is hard, regular, 100 to 160; the temperature is subnormal, but rises toward the end. The coma deepens and death occurs in eight to ten days.

W. G. Archangelsky<sup>52</sup> reports a case of tuberculous meningitis in an 8-year-old child who recovered. Lumbar puncture on admission gave a clear fluid, containing numerous mononuclear cells and tubercle bacilli. On the twenty-third day the fluid was normal.

The writer has made a very careful study of the literature and has found several reports of recovery from tuberculous meningitis. In some cases the diagnosis was substantiated at autopsy, when, the child having died from other causes, healed tubercles were found. In other cases it was

based on the character of the spinal fluid and the finding of tubercle bacilli.

Archangelsky emphasizes the value of lumbar puncture as a therapeutic agent, since, on the one hand, it diminishes the cerebrospinal pressure, and, on the other, eliminates the tubercle bacilli and their toxins.

He says that the rare occurrence of these cases does not alter the prognosis of the disease as it is known, but is of theoretical interest and spurs the physicians further to work out the pathology and therapy of diseases of the meninges in general and tuberculous meningitis in particular.

J. Cassel<sup>53</sup> has observed forty-five cases of tuberculous peritonitis in children. Of these thirty-one were not operated on, eight recovered, nine died, and the fate of the others is not known. Of those operated, six recovered, six died.

Cassel says that if, after a proper general régime has been carried out for weeks, a febrile stage develops with increased swelling of the abdomen and emaciation, he does not hesitate to turn the patient over to the surgeon. But he does not advise operation if hygienic and dietetic treatment cannot be continued after the operation.

The following interesting case of tuberculous peritonitis is reported by A. Galliot:<sup>54</sup> A rachitic child of 6 years had shown signs of tracheo-bronchial adenopathy, mucomembranous enteritis, with meteorism, and slight fever; but for eighteen months he had felt well. On the night of January 8 he showed vague symptoms which were attributed to an indigestion. The following day there was vomiting with pains in the abdomen and a temperature of 38 C. On the tenth the pain became localized in the right iliac fossa. There was decided resistance and tenderness over McBurney's point. A diagnosis of appendicitis was made and the abdomen opened. The peritoneal cavity contained a yellowish fluid. The intestinal coils were adherent, as well as the appendix, which was in the retrocecal fossa. On the peritoneum of the cecum were small calcareous masses and typical tubercles. None occurred on the appendix. The appendix was extirpated and the abdomen closed.

J. H. Bradshaw<sup>55</sup> describes a case of tuberculous peritonitis, due probably to direct intestinal infection. The child, an 18-months-old baby, was well-developed and had never been sick. One day he picked up from the floor a walking-stick and sucked the ferule end. Soon afterward the typical picture of a severe peritonitis sicca developed. Laparotomy was performed, the abdomen being simply opened and closed. Improvement was transitory, then the child failed rapidly. A second operation was performed. Adhesions were broken up and after a futile attempt to free the ileocecal region, which was filled with tubercular

masses, the abdomen was closed again. The child recovered, is now 3 years old, and in good health.

Bradshaw believes tuberculous peritonitis in children arises chiefly from an intestinal infection and that milk is a frequent source of it.

P. Vignard and L. Thévenot<sup>56</sup> discuss tuberculosis of the testicles in children. They report three cases. The first patient was 12 years old. There had been a swelling in the scrotum for about a month. Examination showed a testicle of normal size, but a large nodular indurated epididymus. The vas deferens was also indurated. Epididymectomy and resection of the vas resulted in recovery.

The second patient was a 14-months-old baby. Both testicle and epididymus were involved; a fistula from the testicle discharged a yellow serous pus. Although an operation was performed, the child died six months later.

The third patient was aged 11 months; the testicle, epididymus and vas deferens were all involved. The child died of tuberculous meningitis shortly after the operation.

According to these writers, tuberculosis of the testicles may be primary or secondary. The primary disease differs from that which occurs in adults in involving both testicle and epididymus. The secondary form is much more extensive. It is usually bilateral and involves, besides the testicle and epididymus, the prostate, inguinal, iliac, and lumbar glands.

'The onset may be sudden and acute and suggests an acute gonorrheal orchitis, or may be slow, and remain unsuspected until revealed by chance or by rupture of an abscess.

M. Cabannes<sup>57</sup> reports the history of a child attacked by a primary tuberculosis of the conjunctiva, the result of direct inoculation. She was kissed on the eye by a patient suffering from phthisis and a month later a vegetative, ulcerative conjunctivitis developed, with suppuration of the submaxillary and postcervical glands. As a control for diagnosis, Cabannes inoculated a fragment of the vegetation into the anterior chamber of the eye of a rabbit. The animal developed a keratitis, which healed spontaneously; but three weeks later a tuberculous lesion developed at the point of inoculation.

W. Milligan<sup>58</sup> asserts that tuberculous otitis occurs more frequently than is usually supposed, and, because of its high mortality and the irreparable damage which it does to the ear, it ought to be recognized early and subjected to suitable treatment. The author thinks that 20 per cent. of the children under 6 years of age suffering in the hospitals from a purulent otitis owe the disease to a tuberculous infection. The infection probably passes through the pharyngeal or nasopharyngeal mucosa.

There are no particular subjunctive symptoms pathognomonic of tuberculous otitis. The clinical picture is usually as follows: There is no pain, and examination of the drum reveals no inflammatory reaction, but frequently two perforations or more.

There is early enlargement of the peri-auricular glands and facial paralysis. The discharge is copious, thin, sanious and extremely fetid. The tuberculin reactions are of value, as aids to diagnosis. The prognosis must be guarded, for the death-rate is as high as 50 per cent.

Operative treatment is necessary. If the infection spreads to the glands, tuberculin treatment is advised — 1/10,000 to 1/20,000 mg. controlled by the opsonic index.

#### PROPHYLAXIS

59. Hawes, J. B.: The Tuberculosis Problem as Applied to Children. Boston Med. and Surg. Jour., 1910, clxiii, 904.

60. Kingsley, S.: Open Air Schools in Chicago. Brit. Jour. of Tuberculosis, 1911, v, No. 3.

61. Taylor, D. M.: The Tuberculous School Child with Special Reference to Open Air Schools. Brit. Jour. of Tuberculosis, 1911, v, No. 3.

62. Williams, R.: Sheffield Open Air School. Brit. Jour. of Tuberculosis, 1911, v, No. 3.

63. Wood, F. T. H.: Darlington Open Air School. Brit. Jour. of Tuberculosis, 1911, v, No. 3.

64. Snedden, D.: Open Air Schools. Boston Med. and Surg. Jour., Oct. 26, 1911.

65. Leen, T. F.: Open Air Rooms and Schools, *ibid.*

66. Hawes, J. B.: Open Air Rooms and Schools, *ibid.*

67. Perkins, F.: Fresh Air Schools. Boston Med. and Surg. Jour., Jan. 5, 1911.

68. Locke, E. A., and Murphy, T. J.: Boston Hospital School for Tuberculous Children. Boston Med. and Surg. Jour., Aug. 17, 1911.

69. Woodruff, T. O.: Prevention of Tuberculosis in Children. Jour. Out-Door Life, 1911, viii, 217.

70. Landsberger, J.: Infant Welfare from Standpoint of Campaign Against Tuberculosis. Berl. klin. Wchnschr., 1911, xlviii, No. 27.

J. B. Hawes<sup>59</sup> emphasizes the importance of caring for children with tuberculosis and training them in the right way of living. He deplors the fact that there is no place in Massachusetts where children with open tuberculosis can be cared for and that there are only one or two open-air schools where anemic pretuberculous children can get fresh air and sunshine, in addition to a knowledge of reading, writing and arithmetic.

He suggests that one means of forcing the state and local authorities to provide for these children is to make application for their admission to state sanatoriums. The strongest argument which the board of these institutions can use before the legislature is a long list of applications from children for whom there is no place.

He also suggests earnest and intelligent cooperation with the local school board to provide fresh air rooms for pretuberculous children, and that tuberculosis exhibits should be placed in the schools and demon-

strated by doctors, nurses and social workers to inform the children about the disease and its prevention.

A series of articles has lately been published on open-air schools. In these various institutions the equipment, methods of feeding, examination and teaching are more or less similar. J. Perkins describes the school in Providence, R. I. The exposure of the open side of the room is south. The feet of the children are protected by sitting-out bags, such as are commonly used for tuberculous patients. The children wear caps and mittens. They are given some form of nourishment, e. g., hot milk or soup at 10 o'clock. They bring a lunch with them and eat it at 12 o'clock, having it supplemented by hot cocoa, pudding, or a substantial stew. The lunch is served at a regular table, the children being taught to set the table, clear it, and wash the dishes. They must wash their hands and faces and brush their hair before eating and cleanse their teeth after eating. It is important for the success of the work that the children be visited in their homes and the home conditions studied and improved.

In Boston's hospital school for tuberculous children,<sup>88</sup> besides the incipient cases, more advanced ones were taken. The entire staff consisted of three physicians, a nurse, a social worker, a dietitian, five teachers, a cook, and two maids. The children were divided into three groups. Those in the first were required to follow the regular routine school work. The second group was intermediate. The third was given a minimum amount of study and exercise.

This school has been closed, but the open air rooms in the Boston schools are a direct outcome of the work done there.

#### TREATMENT

71. Escherich, T.: Tuberculin Treatment of Tuberculosis in Childhood. *Wien. med. Wchnschr.*, Jan. 3, 1911.

72. Ager, L. C.: Therapeutic Use of Tuberculin in Intra-Thoratic Tuberculosis of Children. *Am. Jour. Obst.*, February, 1911.

73. Raw, N.: The Treatment of Pulmonary Tuberculosis with Bovine Tuberculin. *Lancet*, London, 1911, No. 180, 929.

74. Gouraud: Tuberculin Therapy in Childhood. *Arch. de méd. des enf.*, 1911, xv, 744.

75. Jochmann, G., and Moellers, B.: Treatment of Tuberculosis with Albumose-Free Tuberculin, *Deutsch. med. Wchnschr.*, 1911, xxxvii, No. 28, 1298.

76. Comby, J.: Recalcification Treatment of Tuberculosis in Children. *Arch. des méd. des enf.*, 1911, xix, 213.

77. Sobotta, E.: Tubercular Predisposition and its Conquest. *Ztschr. f. Tuberk. u. Heilstättenw.*, 1911, xvii, 230.

78. Bernheim, S., and Dieupart, L.: Treatment of Tuberculosis with Radio-active-Iodin Menthol. *Ztschr. f. Tuberk. u. Heilstättenw.*, 1911, vii, 440.

79. Goodall, H. S.: Results of Sanitarium Treatment in Children. *Boston Med. and Surg. Jour.*, 1910, p. 432.

80. Bardenheuer, B.: Sunlight in the Treatment of Surgical Tuberculosis. *Deutsch. Ztschr. f. Chir.*, 1911, cxii, No. 1-3.

81. Joachimsthal, G.: What Paris is doing for Children with Bone and Joint Tuberculosis. *Berlin. klin. Wchnschr.*, 1911, xlviii, No. 8.

T. Escherich<sup>71</sup> believes that the fight between the tuberculous infection and the organism is dependent on the formation of anaphylactic antibodies and on the general resistance of the patient. Escherich suggests the administration of tuberculin, not in large doses, as Schlossman and Engel advise, but in doses just large enough to stimulate the production of anaphylactic bodies. The dose is 0.001 to 0.002 c.mm. injected once or twice a week for two or three months. As this dose is seldom followed by a rise in temperature or untoward symptoms, it can be advantageously used in an ambulatory clinic. After the first or second injection the general condition is usually improved. After being treated two months the children should be sent to the country. Escherich has given this method a thorough trial and has met with satisfactory results. He does not use it with patients in advanced stages, but in those who are brought with indefinite signs of the disease, as pallor, loss of appetite, general debility, loss of weight, and a positive v. Pirquet reaction.

In conclusion, he says, if tuberculin is to have a permanent place in the treatment of tuberculosis of childhood, it must not be used, as it formerly was, as a last resort, but in latent or incipient cases, and should be given in carefully regulated doses.

According to L. C. Ager,<sup>72</sup> the curative effects of tuberculin are due to the stimulation of the body cells and not to any direct action on the tuberculous focus. The type of cases in which tuberculin is most useful are the chronic ones which do not yield to ordinary treatment. Under hygienic treatment patients of this class improve, but sooner or later suffer a return of symptoms with increased physical findings.

The organism needs stimulation, which is effected by the use of tuberculin. It is best given in small doses, 1/5,000 or 1/1,000 mg. daily, for a period of ten days, or two weeks. The daily dose is increased, but must not exceed 0.01 mg. After such a course of treatment there is usually a definite and progressive improvement for several months, then an exacerbation, but much slighter than before the tuberculin treatment. This is an indication for another period of tuberculin treatment. Three or four such courses ordinarily bring about a cure. Patients should be in a sanatorium or hospital and also receive the usual outdoor and hygienic treatment.

N. Raw<sup>73</sup> advises the use of bovine tuberculin in the treatment of tuberculosis. He says it is less irritating and less likely to produce reactions when given in large doses.

Gouraud<sup>74</sup> believes that tuberculin is of great service in treating tuberculosis of children, especially in scrofula, bone and glandular tuberculosis, and tuberculous cachexia, but it is useless in pulmonary tuberculosis. Initial doses are 0.001 to 0.01 mg., which can be rapidly increased to a gram.

G. Jochmann and B. Moellers<sup>75</sup> use a tuberculin which is obtained by growing the tubercle bacillus on a medium deprived of albumose. The authors maintain that this tuberculin is less toxic than the old tuberculin, causes little or no reaction, and can be increased rapidly in dosage.

J. Comby<sup>76</sup> discusses Ferrier and Sergent's recalcification method of treating tuberculosis in children. This seeks to combat the calcium excretion and to introduce into the organism salts of calcium capable of being fixed in the tissues. In the first place, the dyspepsia so frequent in overfed tuberculous patients is corrected by lengthening the interval between meals and regulating the diet. Foods usually given dyspeptic children are allowed, as milk dishes, eggs, boiled fish, grilled or roasted meats, purees of vegetables, dried fruits, toasted or dry bread. Fats, alcoholic drinks, foods easily fermentable, like cheese, are forbidden. Calcium-containing mineral waters are given freely. The following tablet is given between meals:

	Gm.
Calcium carbonate .....	0 30
Tricalcium phosphate .....	0 50
Sodium chlorid .....	0 15
Calcined magnesia .....	10 00

Cod-liver oil, acid medicaments and syrups are rigorously forbidden. Alternating with the tablets, arsenate of soda is prescribed as follows: The child takes twenty tablets in ten days; then for six days a teaspoonful of the following: arsenate of soda, 0.03 gm., aquæ, 100 c.c. Then the tablets again.

Comby speaks highly of this treatment, although he emphasizes the fact that hygienic treatment must not be forgotten, but must be placed first.

According to E. Sobotta,<sup>77</sup> the assertions of the French writers regarding demineralization in tuberculosis has been confirmed by other writers. Phosphaturia and softening and caries of the teeth are evidence of this demineralization. Sobotta calls attention to the fact that tuberculosis is rare in regions where the water has a high calcium salt content. He believes that lime should not only be given freely to tuberculous patients, but that a predisposition to the disease should be fought by the administration of lime salts.

S. Bernheim and L. Dieupart<sup>78</sup> treated seventy-five patients with tuberculosis with Szendeffy's radio-active iodine menthol solution. The preparation consists of the following: peptonized iodine, 0.75; menthol, 0.06; radium barium chlorid, one-tenth of a drop in ether solution. Each day 1 c.c. of the solution was injected deep into the muscles for thirty days, then repeated two or three times after an interval of fourteen days.

No intolerance of the drugs was shown even in children. The writers are very enthusiastic about their results. Gain in weight was constant, the appetite increased, and the expectoration diminished.

H. S. Goodall<sup>79</sup> summarizes the results in the treatment of tuberculous children at Stoney Wold Sanitarium during the first six years of its existence. In all, 120 children were discharged. The results were better than those obtained among adults under the same conditions. All who were discharged as apparently cured or with the process arrested, at present are as well as when discharged, or better. The author found that little girls between 6 and 12 years yielded more readily to treatment than any other group. Boys between 13 and 16 show a percentage of good results above the girls of the same age and come next to the little girls.

B. Bardenheuer<sup>80</sup> tried the effect of systematic sunlight in the treatment of surgical tuberculosis and his experience has convinced him that far better ultimate results can be obtained with sunlight without mutilating operations. Bardenheuer had the lesions exposed to sunlight for fifteen minutes three times a day, rapidly increasing to two or three hours morning and afternoon, or all day long except in midwinter. As he had no facilities for sun baths, he simply had the patients placed at the open window, where the sun could reach the lesion.

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## PATHOLOGY

### Enteroptosis in Children

(R. R. Smith, *Journal A. M. A.*, February 10, 1912, p. 385.)

After reference to a former paper in *The Journal* (Nov. 26, 1910, p. 1860), and redescribing the symptomatology of the enteroptotic woman of the true or non-acquired type, Smith says that careful inquiry as to the history of the well-developed cases will trace it back to early childhood, i. e., they will tell you they were thin, pale and perhaps more or less nervous even at that early period. He has since studied 109 female children ranging in age from birth to 13 years. The height was obtained and, following the routine used with adults, the size of the middle zone of the trunk was estimated by obtaining the index of Becher and Lenhoff, which gives the relative capacity of the upper abdomen in a general way. This is obtained by dividing the jugulopubic distance by the waist circumference and multiplying the result by 100. After this the general state of nutrition is observed, the attitude of the child, the size and shape of the thorax and the epigastric angle. The kidneys were palpated where possible and the position of the lower border of the stomach determined by the gas method and percussion. Some examinations were necessarily incomplete. A number of photographs were obtained and in twenty-four cases the  $x$ -ray was used. He was also enabled, through the kindness of Dr. R. W. Lovett, to examine a number of children in the various Boston institutions, but his work was done largely in the D. A. Blodgett Home for Children in Grand Rapids. From his study he concludes that the enteroptotic



habit of adult life is seen in its fundamental characteristic in the frail child—frailness, lack of fat, slenderness of muscle and lack of vigor in bodily development. The actual collapse of the thorax and the lessened capacity of the upper abdomen is observable only in the older children, and then only exceptionally, but the muscular insufficiencies of later life are common in frail children. The prolapse of the kidneys, stomach, colon and the intestines, which is seen in the adult, is not pronounced in children under 12 except in rare instances and then only as a late development. He thinks that the consequences of this condition in childhood are chiefly seen in the adult and much can be done to prevent them. If this can be uniformly done there will be many less weak and physically incompetent women.

## INDEX OF CURRENT PEDIATRIC LITERATURE

### ANATOMY, PHYSIOLOGY AND HYGIENE

- Duties of State and Municipalities in Prevention of Infant Mortality. C. L. Patterson.  
Ohio Med. Jour., January, 1912.
- Hospitals for Care of Infants and Children and Methods of Prevention of Infection. H. Koplik.  
Arch. Pediat., January, 1912.
- Infant Welfare Movement. T. B. Cooley, M.D., Detroit, Mich.  
Detroit Med. Jour., January, 1912.
- Infant Welfare Stations. (De l'éducation des nourrices et de la surveillance des nourrissons.) E. Vidal.  
Bull. de l'Acad. de méd., Paris, Dec. 19, 1911.
- Medical Inspection of Schools and School Children. J. B. Story.  
Dublin Jour. Med. Sc., January, 1912.
- Neurotic Basis of Juvenile Delinquency, With a Study of Some Special Cases, Mostly from the San Francisco Juvenile Court. P. K. Brown.  
Jour. Am. Med. Assn., Jan. 20, 1912.
- Recent Legislation and its Bearing on Infant Life. A. J. Horne.  
Dublin Jour. Med. Sc., January, 1912.
- Relation of Social and Economic Conditions to Infant Morbidity and Mortality. J. Levy.  
Arch. Pediat., January, 1912.
- Results of Measures for Infant Welfare. (Statistik der Erfolge von Fürsorgemassnahmen.) G. Tugendreich.  
Arch. f. Kinderh., 1912, lvii, Nos. 1-3.
- Treatment of Stuttering and Stammering and Voice Defects Through Science and Art of Speech and Singing. B. Cadwallader.  
Cleveland Med. Jour., December, 1911.
- Value of Health Department in Los Angeles City Schools. A. W. Moore.  
South. California Pract., January, 1912.
- Work of Babies' Class During Year Ending Oct. 1, 1911. E. L. Coolidge.  
Bull. Lying-In Hosp. New York, June, 1911.

### PATHOLOGY AND BACTERIOLOGY

- Cancer of Ovary in Girl Aged Eleven Years. F. H. Lahey and S. R. Haythorn.  
Am. Jour. Med. Sc., February, 1912.
- Enlargement of Thymus: Remarkable Case. A. M. Kennedy.  
Glasgow Med. Jour., lxxvii, 1.
- Experimental Research on Involution of the Thymus under Exposure to the Roentgen Rays. (Sur l'involution du thymus produite par les rayons X.) C. Regaud and R. Cremieu.  
Lyon Médical, Jan. 7, 1912.
- Giant Children. (Riesenkinder). M. Oyamada.  
Beitr. z. Geburtsh. u. Gynäk., 1912, xvii, No. 1.
- Infantilism. M. de Biehler.  
Arch. de méd. des Enf., January, 1912.
- Infantilism. (Zur Begriffsbestimmung des Infantilismus.) B. Wolff.  
Arch. f. Kinderh., 1912, lvii, Nos. 1-3.

- Latent Hypertrophy of the Thymus. (Les hypertrophies thymiques latentes et les "petits signes" de l'hypertrophie du thymus). D'Oelsnitz.  
Bull. de Soc. de Pédiat., December, 1911.
- Management of Inguinal Hernia in Childhood. W. F. Campbell.  
Med. Rec., New York, Jan. 20, 1912.
- Physical Evidences of the Thymus. C. Basch and A. Rohn. Translated by A. C. Soper, Jr.  
Am. Jour. Dis. Child., February, 1912.
- Roentgenoscopy of Hypertrophy of the Thymus. (Les caractères de l'image radioscopique dans l'hypertrophie du thymus.) D'Oelsnitz and Paschetta.  
Bull. de Soc. de Pédiat., December, 1911.
- Very Young Embryo in Accessory Tube. (Ueber ein junges menschliches Ei im Mesosalpingiolium einer Nebentube.) M. Watthard.  
Ztschr. f. Geburtsh. u. Gynäk., 1912, lxi, No. 3.

### METABOLISM AND NUTRITION

- Advantages of Malt Sugar Over Lactose in Infant Feeding. F. C. Neff.  
Med. Herald, January, 1912.
- Arthritis in Children and Elimination of Uric Acid. ("Arthritismus im Kindesalter und Harnsäure-Ausscheidung.") A. Uffenheimer.  
Monatschr. f. Kinderh., 1912, x, No. 9.
- Cell Content of Milk. H. E. Ross.  
Jour. Infec. Dis., January, 1912.
- Desiccated Milk in Infant Feeding. (Poudre de lait ou lait sec dans l'alimentation des enfants). E. C. Aviragnet, Bloch-Michel and Dorlencourt.  
Bull. de Soc. de Pédiat., December, 1911.
- Diabetes Mellitus in Childhood. W. Gellhorn.  
Northwest Med., January, 1912.
- Difficulties in Breast Feeding. G. S. Strathy. M.D.  
Canadian Pract. and Rev., February, 1912.
- Feeding and Care of New-Born Infants. (Neue Erfahrungen in der Technik der Ernährung sowie zur Physiologie und Pflege des Neugeborenen.) R. T. Jaschke.  
Monatschr. f. Geburtsh. u. Gynäk., January, 1912.
- Is Milk of Eclamptic Mothers Toxic? C. A. Frost.  
Arch. Pediat., January, 1912.
- Modern Problems in Infant Feeding. H. L. K. Shaw.  
Albany Med. Ann., January, 1912.
- Research on Metabolism of Normal Artificially Fed Infant. (Der Gesamtstoffwechsel eines künstlich genährten Säuglings. Mit Einschluss des respiratorischen Stoffwechsels). A. Niemann. Concluded.  
Jahrb. f. Kinderh., December, 1911.
- Salt Fever. (Zur Theorie des Kochsalzfiebers). M. Katzenellenbogen.  
Monatschr. f. Kinderh., 1912, x, No. 9.
- Study of the Pyrogenic Action of Lactose. F. W. Schlutz.  
Am. Jour. Dis. Child., February, 1912.

### DISEASES OF THE NEWLY-BORN

- Ancient Work on the Diseases of the Newly-Born. (Un livre sur les maladies des nouveau-nés écrit vers 1472). E. Apert.  
Arch. de méd. des enf., January, 1912.
- Intracranial Hemorrhage in the Newly-Born. (Ueber die Genese intrakranieller Blutungen bei Neugeborenen). L. Seitz.  
Zentralb. f. Chir., Jan. 6, 1912.
- Laceration of Tentorium During Birth. (Tentoriumzerreissungen bei der Geburt.) R. Pott.  
Ztschr. f. Geburtsh. u. Gynäk., 1912, lxi, No. 3.

- Omphalorrhagia Neonatorum. J. H. Richards.  
Med. Rec., New York, Jan. 13, 1912.
- Preventable Cause of Death in Early Infancy. E. V. Davis.  
Jour. Oklahoma Med. Assn., January, 1912.
- Sclero-Edema of New-Born Infants. (Beitrag zum Sclerödema neonatorum.)  
E. Geiser.  
Monatschr. f. Geburtsh. u. Gynäk., January, 1912.
- Young Human Embryo. (Ein junges menschliches Ei.) R. Todyo.  
Arch. f. Gynäk., 1912, xcv, No. 2.

### ACUTE INFECTIOUS DISEASES

- Acute Poliomyelitis in California. F. F. Gundrum.  
Jour. Am. Med. Assn., Jan. 27, 1912.
- Acute Poliomyelitis in Iowa. W. L. Bierring.  
Interstate Med. Jour., January, 1912.
- Analysis of 312 Cases of Laryngeal Diphtheria; Outline of Treatment. F. V. Scholes.  
Australian Med. Jour., Dec. 16, 1911.
- Autoserotherapy in Two Cases of Subacute Cerebrospinal Meningitis With Cure.  
O. H. Brown.  
Jour. Missouri Med. Assn., January, 1912.
- Bronchopneumonia. H. L. Shaw.  
Jour. South Carolina Med. Assn., January, 1912.
- Case of Acute Purulent Arthritis in Child of Ten Months, With Radiograph. J. Burfield and A. J. Cleveland.  
Brit. Jour. Child. Dis., January, 1912.
- Complications with Typhoid. (Komplikationen bei Typhus abdominalis.)  
Schuster.  
Med. Klin., Jan. 14, 1912.
- Diazo Reaction in Scarlet Fever and Serum Sickness. S. S. Woody and J. A. Kolmer.  
Arch. Pediat., January, 1912.
- Diphtheria. W. W. Harper.  
South. Med. Jour., January, 1912.
- Diphtheria Bacilli Carriers and Persistence of the Bacilli. (Zur Epidemiologie der Diphtherie). P. Somerfeld.  
Arch. f. Kinderh., 1912, lvii, Nos. 1-3.
- Diphtheria Carriers in School Epidemic; Treatment. G. Leary.  
Australian Med. Jour., Dec. 16, 1911.
- Diphtheria of Esophagus. J. D. Rolleston.  
Brit. Jour. Child. Dis., January, 1912.
- Early Diagnosis and Treatment of Meningitis. C. J. Fishman.  
Jour. Oklahoma Med. Assn., February, 1912.
- Epidemic Cerebrospinal Meningitis.  
Editorial Jour. Am. Med. Assn., Feb. 3, 1912.
- Epidemic Poliomyelitis with Bulbar Symptoms. (Bulbare Form der epidemischen Kinderlähmung). E. Müller.  
München. med. Wehnschr., Jan. 23, 1912.
- Epidemiology and Early Diagnosis of Measles. (Zur Epidemiologie und Frühdiagnose der Masern.) P. Rohmer.  
Jahrb. f. Kinderh., January, 1912.
- Generalized Infection with Diphtheroid Organism. L. M. DeWitt.  
Jour. Infect. Dis., January, 1912.
- Infantile Paralysis; Etiology and Pathology. P. Hilkowitz.  
Colorado Med., January, 1912.
- Infantile Paralysis; Prophylaxis and Treatment. J. W. Ames.  
Colorado Med., January, 1912.

- Influenza and Cerebrospinal Meningitis. J. H. L. Cumpston.  
Australasian Med. Gaz., Jan. 6, 1912.
- Optic Neuritis Following Measles. J. M. Griscom.  
Ann. Ophth., January, 1912.
- Pneumococcal Meningitis. H. Drummond.  
British Med. Jour., Jan. 27, 1912.
- Prophylaxis of Scarlet Fever and Diphtheria Among School Children. (Zur gegenwärtigen Scharlach- und Diphtherieepidemie in Gross-Berlin.) M. Westenhoeffer.  
Berlin. klin. Wchnschr., Jan. 8, 1912.
- Protracted Cerebrospinal Meningitis and Recovery After Decompressive Trephining. (Méningite cérébro-spinale prolongée à forme cachectisante.) R. Debré.  
Ann. de méd. et chir. inf., Jan. 15, 1912.
- Raspberry Tongue in Children. (Ueber die Himbeerzunge der Kinder). G. E. Wladimiroff.  
Arch. f. Kinderh., 1912, lvii, Nos. 1-3.
- Rheumatism in Children. A. M. Gossage.  
The Practitioner, January, 1912.
- Serotherapy of Tetanus; Two Cases. (Tetanus traumaticus mit Antitoxin Höchst und Blutserum einer geheilten Tetanuskranken geheilt). A. Wiedemann.  
München. med. Wchnschr., Jan. 23, 1912.
- Serous Meningitis. K. Weiss.  
Centralbl. f. d. Grenzgeb. d. Med. u. Chir., Dec. 21, 1911.
- Subsidence of Infiltrations After Acute Infections in Children. (Heilung von Infiltrationen im Kindesalter nach akuten Infektionen.) E. Baumgartern.  
Med. Klinik, Jan. 7, 1912.
- Surgical Treatment of Paralysis Following Anterior Poliomyelitis. N. Allison.  
Jour. Missouri Med. Assn., January, 1912.
- Two Recurrences of Measles. (Ein doppeltes Masernrecidiv.) Feibelmann.  
Arch. f. Kinderh., 1912, lvi, Nos. 1-3.

#### TUBERCULOSIS AND SYPHILIS

- Craniotabes and Syphilis. J. Roux.  
Bull. de Soc. de Pédiat., December, 1911.
- Morbid Findings in Umbilical Cord in Syphilis. (Alterationen des Nabelstranges bei Syphilis.) M. Dominici.  
Virchow's Arch. f. path. Anat., December, 1911.
- Mortality and Morbidity in Hereditary Syphilis. C. F. Marshall.  
Brit. Jour. Child. Dis., January, 1912.
- Salvarsan in Inherited Syphilis. (Erfahrungen mit Salvarsan bei Lues congenita.) E. Welde.  
Jahrb. f. Kinderh., January, 1912.
- Serodiagnosis of Inherited Syphilis in Children and of Familial Syphilis. (Le sérodiagnostic dans l'hérédosyphilis infantile et la syphilis familiale). C. Leroux and R. Labbé.  
Arch. de méd. de Enf., December, 1911.
- Treatment of Tuberculous Adenitis. J. B. Hawes.  
Boston Med. and Surg. Jour., Jan. 18, 1912.

#### DIGESTIVE SYSTEM

- Acute Yellow Atrophy of Liver in Children. Report of Case. J. Phillips.  
Am. Jour. Med. Sc., February, 1912.
- Aphthæ in Children. (Les aphtes chez l'enfant.) E. Gaujoux.  
Ann. de méd. et chir. inf., January, 1912.
- Atresia of Duodenum Fatal in One Week After Birth. (Atresia duodeni als Todesursache bei einem Neugeborenen von 7 Tagen). H. Hauser.  
Monatschr. f. Geburtsh. u. Gynäk., December, 1911.

- Case of Intussusception Complicated by Volvulus. C. S. Lawrence.  
 Jour. Am. Med. Assn., Jan. 6, 1912.
- Chemical Studies on Intestinal Infantilism. F. H. McCrudden.  
 Jour. Exper. Med., February, 1912.
- Chronic Invagination of the Intestine in Boy of 4 Mistaken for Dysentery. J. Comby.  
 Arch. de méd. des Enf., January, 1912.
- Congenital Stenosis of Pylorus. R. C. Smedley.  
 Northwest Med., January, 1912.
- Depressing Action of Hot Weather on Gastric Secretion. (Die Einwirkung hoher Aussenlufttemperaturen auf die sekretorische Tätigkeit des Magens). V. Salle.  
 Jahrb. f. Kinderh., December, 1911.
- Intestinal Invagination. (Rapport sur deux observations d'invagination intestinale par le Dr. P. Grisel). L. Ombredanne.  
 Bull. de Soc. de Pédiat., December, 1911.
- Intestinal Obstruction, With Special Reference to Intussusception in Infants. O. O'Neil.  
 Yale Med. Jour., December, 1911.
- Megacolon. (Zur Diagnose und Therapie der Hirschsprung'schen Krankheit). H. Hoffmann.  
 Beitr. z. klin. Chir., November, 1911.
- Pathogenesis of Digestive Disturbances in Infants (Die qualitativ-quantitative Bestimmung flüchtiger Fettsäuren in den Destillaten der Vakuum-Dampfdestillation). F. Edelstein and F. v. Csonka.  
 Ztschr. f. Kinderh., 1912, iii, No. 4.
- Pyloric Obstruction in Infants with Muscular Hypertrophy at the Pylorus. W. B. Lewitt and L. Porter.  
 Jour. Am. Med. Assn., Jan. 27, 1912.
- Purpura in Infective Diarrhea. H. D. Rolleston and J. B. Molony.  
 Brit. Jour. Child. Dis., January, 1912.
- Reactive New-Growth in Cirrhosis of the Liver. (Zur Frage der reaktiven Neubildungsvorgänge bei Lebercirrhose). A. Czerny.  
 Monatschr. f. Kinderh., 1912, x, No. 9.
- Significance and Treatment of Vomiting in Infants and Children. H. Lowenburg.  
 Jour. Am. Med. Assn., Jan. 20, 1912.
- Stenosis and Hypertrophy of the Pylorus in Two Infants. (Zwei Fälle von hypertrophischer Pylorusstenose beim Säugling.) T. Tanaka.  
 Jahrb. f. Kinderh., January, 1912.
- Surgical Treatment of Congenital Hypertrophic Stenosis of Pylorus. R. T. Richards.  
 Northwest Med., January, 1912.

#### RESPIRATORY SYSTEM

- Drainage of Acute Pleural Empyema in Children. S. W. Kelley.  
 Am. Jour. Surg., January, 1912.
- Means for Artificial Respiration for Children. (Eine Methode der künstlichen Atmung bei Kindern). Saokolow.  
 Monatschr. f. Kinderh., 1912, x, No. 9.
- Plastic Bronchitis. (Bronchitis plastica). P. Schneider.  
 Jahrb. f. Kinderh., January, 1912.
- Spirometric Research on Children's Respiration. (Spirometrische Untersuchungen zur Pathologie und Pharmacologie der Atmung im Kindesalter). R. Lederer and H. Vogt.  
 Jahrb. f. Kinderh., January, 1912.
- Thymic Death and Thymic Asthma in Children. (Mors thymica et Asthma thymicum bei Kindern). D. Saokolow.  
 Arch. f. Kinderh., 1912, lvii, Nos. 1-3.

**BLOOD AND CIRCULATORY SYSTEM**

- Arhythmia Induced by Manipulation of Abnormally Located Heart. (Arythmie provoquée chez l'homme par l'excitation manuelle du cœur à travers la paroi abdominale, chez un sujet à cœur ectopié.) D. Danielopolu.  
Arch. des Malad. du Cœur., January, 1912.
- Biologic Research on Maternal and Umbilical Blood. (Biologische Studien über mütterliches und Nabelschnurblut). E. v. Graff and J. von Zubrzycki.  
Arch. f. Gynäk., 1912, xcv, No. 3.
- Epidemic Occurrence of Acute Heart Disease in Children. (Ueber gehäuftes Auftreten von akut entzündlichen Herzerkrankungen im Kindesalter.) A. Forell.  
München. med. Wehnschr., Jan. 16, 1912.
- Heart Sounds in Infants. (Herztöne kranken und gesunder Säuglinge). W. Schlieps.  
Monatschr. f. Kinderh., 1912, x, No. 9.
- Injection of Blood or Serum for Hemorrhage and Anemia. (Ueber therapeutische Erfolge bei Blutungen, hämorrhagischer Diathese und perniziöser Anämie durch Injektion von Serum besw. defibriniertem Blut Gesunder.) M. John.  
München. med. Wehnschr., Jan. 23, 1912.
- The Polygraph as an Aid in Diagnosis of Cardiac Conditions in Children. G. R. Pisek and H. T. Coffen.  
Am. Jour. Dis. Child., February, 1912.
- Sigmoid Sinus and Jugular Bulb in Infancy. W. C. Braislin.  
Laryngoscope, December, 1911.
- Treatment of Acute Endocarditis and Myocarditis. F. S. Meara.  
Jour. Am. Med. Assn., Feb. 3, 1912.

**NERVOUS SYSTEM**

- Acute Articular Rheumatism in Child Causing Acute Mental Confusion. Salicylic Acid Refound in Cerebrospinal Fluid. (Rhumatisme cérébral à forme de confusion mentale aigue.) P. Nobécourt and H. Darre.  
Bull. Soc. de Pédiat., November, 1911.
- Bilateral Spastic Paralysis in Children. (La maladie de Little. Etiologie, pathogénie et anatomie pathologique). V. Hutinel and L. Baboneix.  
Ann. de méd. et chir. inf., January, 1912.
- Binet Tests for Mental Retardation. (Les tests de Binet dans le tout jeune âge). R. Cruchet.  
Jour. de méd. de Bordeaux, Jan. 7, 1912.
- Case of Myatonia Congenita. J. R. Charles.  
Brit. Jour. Child. Dis., January, 1912.
- Decompressive Trephining for Children. Broca.  
Bull. Soc. de Pédiat., November, 1911.
- Dietetic Treatment of Infantile Tetany. C. G. Grulee.  
Arch. Pediat., January, 1912.
- Emotional Influences on Disturbances in Speech. (Du rôle de l'émotion en pathologie verbale bégaiement, blésité.) Chervin.  
Semaine Méd., Jan. 24, 1912.
- Infantilism in Hypophysis Disease. A. W. Hewlett.  
Arch. Int. Med., January, 1912.
- Insanity in Children. C. Holmes.  
New York Med. Jour., Feb. 10, 1912.
- Parental Alcoholism as Factor in Mental Deficiency of Children. A. Gordon.  
Month. Cyclo. and Med. Bull., January, 1912.
- Psychology of Children. (Una obra de psicologia infantil.) J. Ingegnieros.  
Samana Medica, Jan. 4, 1912.

Section of Posterior Spinal Nerve Roots for Relief of Spastic Conditions and Sensory Crises. (Zur Förster'schen Operation: Spastische Zustände und sensible Krisen (Tabes) durch Resektion der hinteren Stränge des Rückenmarks zu bessern). B. Heile.

München. med. Wchnschr., Jan. 16, 1912.

Symptomatology of New Growths in Distal Portion of Spinal Cord. (Zur Symptomatologie der Neubildungen am Conus und der Cauda equina). L. Jacobsohn.

Deutsch. med. Wchnschr., Jan. 25, 1912.

Treatment of Spina Bifida. W. Brodmann.

Beitr. z. klin. Chir., November, 1911.

### GENITO-URINARY SYSTEM

Acute Nephritis in Children. (Akute Nephritis in den Kinder- und Jugendjahren mit besonderer Berücksichtigung der Prognose). H. Ernberg.

Nord. med. Ark., 1912, xlv, No. 2.

Colon Bacillus Infection of Urinary Tract in Infants and Children. C. K. Johnson.

Vermont Med. Month., January, 1912.

Cystitis in Male Infants. (Zur Aetiologie der Cystitis bei Knaben im Säuglingsalter). E. Rach and A. v. Reuss.

Jahrb. f. Kinderh., December, 1911.

Treatment of Nocturnal Enuresis in Children. J. Ruhräh.

Am. Jour. Med. Sc., February, 1912.

### OSSEUS SYSTEM

Acute Osteomyelitis in Infants. (Osteomyélite aigue du maxillaire supérieur chez le nourrisson.) R. Français.

Arch. de méd. des enf., January, 1912.

Congenital Dislocation of the Patella. (Ueber kongenitale Patellarluxationen). M. Fiebach.

Beitr. z. klin. Chir., November, 1911.

Indications for Surgical Interference in Treatment of Tuberculous Joint Diseases in Children.

Lancet, London, 1912, i, 1.

Nature of Rachitis and Osteomalacia. M. Ogata.

Beitr. z. Geburtsh. u. Gynäk., 1912, xvii, No. 1.

Rachitic Osteomalacia. (Beitrag zu den klinischen und pathologischen Untersuchungen bei der rachitischen Osteomalacie). M. Ogata, K. Minakuchi and K. Kaji.

Beitr. z. Geburtsh. u. Gynäk., 1912, xvii, No. 1.

### SKIN AND APPENDAGES

Diffuse Edematous Scleroderma Benefited by Thyroid Treatment. E. Apert and Leblanc.

Bull. de Soc. de Pédiat., December, 1911.

Etiology of Impetigo and Eczematous Conjunctivitis. W. Pick.

München. med. Wchnschr., Jan. 23, 1912.

Retention of Chlorids with Exudative Cutaneous Disease. (Chlorretention bei exsudativen Prozessen der Haut). V. Menschikoff.

Monatschr. f. Kinderh., 1911, x, No. 9.

Salt-Free Dietetic Treatment of Eczema in Infants. (Zur Indikation und Technik der Behandlung des Säuglingsekezes mit molkenarmer Milch). H. Finckelstein.

Therap. Monatsh., January, 1912.



- Specific Treatment of Ringworm and Allied Mycoses. (Die Trichophytien und verwandte Pilzkrankungen der Haut). B. Bloch.  
Cor.-Bl. f. schweiz. Aerzte, Dec. 20, 1911.
- Superheated Air in Treatment of Infantile Eczema. (Heissluftbehandlung der Ekzeme im Säuglingsalter). J. Perlmann.  
München. med. Wchnschr., Jan. 9, 1912.

# EYE, EAR, NOSE AND THROAT

- Acute Suppurative Otitis Media. G. H. Ward.  
Jour. Med. Soc. New Jersey, January, 1912.
- Civic Medical Inspection of School Children With Special Reference to Diseases of Eye, Ear and Throat. S. C. Ayres.  
Jour. Ophth. and Oto-Laryngol., January, 1912.
- Dentition Disturbances. (Dentitionskrankheiten). K. Hoffendahl.  
Med. klin., Jan. 14, 1912.
- Eye Strain Among Public School Children. E. Bates.  
Ophthalmology, January, 1912.
- Faucial Tonsil; Anatomic Reasons for Its Capacity for Evil; Some Indications for Its Removal. W. G. Harrison.  
South. Med. Jour., January, 1912.
- Influence of Eustachian Tube in Purulent Otitis. M. D. Ritchie.  
Pennsylvania Med. Jour., January, 1912.
- Lane Operation for Cleft Palate. M. T. Sudler.  
Jour. Kansas Med. Soc., January, 1912.
- Management of Squint in Children. C. W. Le Fever.  
Am. Jour. Dis. Children, February, 1912.
- Non-Surgical Treatment of Chronically Discharging Ears. W. A. Wells.  
Jour. Am. Med. Assn., Feb. 3, 1912.
- Retrospect of Otology, 1911. M. Yearsley.  
Brit. Jour. Child. Dis., January, 1912.
- Some Facts General Practitioners Ought to Know About Tonsils and Tonsil Operations. J. R. Winslow.  
Maryland Med. Jour., January, 1912.
- Suppuration of Middle Ear with Some of Its Complications. S. H. Large.  
Cleveland Med. Jour., December, 1911.
- Technic for Laryngologic Examination. (Une méthode trop peu connue et pourtant indispensable en laryngologie chez l'enfant). H. Abrand.  
Bull. Soc. de Pédiat., November, 1911.
- Tonsillectomy. L. T. Royster.  
Virginia Med. Semi-Month., Jan. 12, 1912.
- Tonsillectomy with a Single Instrument, the Tonsillectome. J. C. Beck.  
Jour. Am. Med. Assn., Jan. 27, 1912.
- Tonsils. E. R. Carpenter.  
New Mexico Med. Jour., January, 1912.

# THERAPEUTICS

- Anaphylaxis in Its Relation to Pediatric Practice. G. R. Pisek and M. C. Pease.  
Boston Med. and Surg. Jour., Jan. 25, 1912.
- Calcium Sulphid in Infectious Diseases. J. E. Pratt.  
Jour. Med. Soc. New Jersey, January, 1912.
- Case of Belladonna Poisoning in Child Seven Years of Age. R. E. Coughlin.  
New York Med. Jour., Jan. 27, 1912.
- Fatal Anaphylaxis after Injection of Serum. (Serumtod infolge von Anaphylaxie). J. Dreyfuss.  
München. med. Wchnschr., Jan. 23, 1912.
- Fatal Case of Bismuth Paste Poisoning. L. W. Ely.  
Med. Rec., New York, Jan. 13, 1912.

- Urethan in Pediatrics. (Verwendbarkeit des Urethans in der Kinderheilkunde).  
F. Bertling.  
Berlin. klin. Wehnschr., Jan. 22, 1912.

#### SURGERY

- Anesthesia in Surgery of Childhood. F. W. Pinneo.  
Arch. Pediat., January, 1912.  
Double Coxa Vara with Other Deformities Occurring in Brother and Sister. L. E. Barrington-Ward.  
Lancet, Jan. 20, 1912.  
Injuries to Elbow in Childhood, Studied in Relation to Development of Joint.  
W. S. Lawrence.  
Surg., Gynec., and Obst., January, 1912.  
Origin of Torticollis: Case Showing Professional Dyskinesia. T. A. Williams.  
New Orleans Med. and Surg. Jour., January, 1912.  
Prevention of Flat-Foot in Children. (Verhütung des Plattfusses im kindlichen Alter). G. Muskat.  
Arch. f. Kinderh., 1912, lvii, Nos. 1-3.  
Treatment of Cicatricial Deformity. (Zur Behandlung der Hautnarben). O. Thilo.  
München. med. Wehnschr., Jan. 23, 1912.  
Treatment of Congenital Talipes in Infants. R. W. Billington.  
Jour. Tennessee Med. Assn., January, 1912.  
Ultimate Outcome of Congenital Dislocation of the Hip-Joint Given Bloodless Treatment. (Du pronostic éloigné des luxations congénitales de la hanche opérées par la méthode non sanglante). P. Redard.  
Ann. de méd. et chir. inf., January, 1912.

#### MISCELLANEOUS

- Diseases of Children. A. J. Wood.  
Australian Med. Gaz., Jan. 6, 1912.  
Pediatric Memoranda. H. B. Sheffield.  
Med. Rec., New York, Jan. 27, 1912.

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## STUDIES OF RECURRENT OR PERIODICAL VOMITING

### A. THE CREATININ AND CREATIN EXCRETION IN RECURRENT VOMITING

#### B. THE RELATION OF ADENOIDS TO RECURRENT VOMITING \*

J. P. SEDGWICK, M.D.

MINNEAPOLIS

#### A. CREATININ AND CREATIN EXCRETION

The older methods of determination of creatinin and creatin were very tedious and unsatisfactory. It was in 1904 that Folin published his accurate and simple method, which has given such an impetus to the study of the creatinin and creatin metabolism. Folin's method depends on the fact that creatinin gives, with picric acid and sodium hydrate, a brownish-red color which cannot be distinguished from that of a potassium bichromate solution. The urine is treated with the above reagents in proper quantity and the resulting depth of color compared with that of a half normal bichromate solution by means of a colorimeter, preferably that of Dubosc. From this reading, by a simple computation, the amount of creatinin is given. If before this process the urine be boiled with normal hydrochloric acid, creatin, if present, is converted into creatinin and the final reading will give creatinin plus the creatin which has been converted into creatinin.

It has been shown by Folin that the creatinin excretion of an adult individual is remarkably constant. The amount excreted is, according to Hoogenhuyze and van Verploegh,<sup>2</sup> little affected by hard muscular exercise or by a protein diet. The creatinin output seems to be an indicator of endogenous nitrogen metabolism (Folin).

Fever increases the creatinin output, as shown by Hoogenhuyze and van Verploegh.<sup>2</sup> Edward Mellanby<sup>3</sup> has endeavored to prove that the liver is the center about which creatin metabolism plays. It is of interest

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1. Folin: *Ztschr. f. physiol. Chem.*, 1904, xli, 223; *Am. Jour. Physiol.*, 1905, xiii, 48.

2. Hoogenhuyze and Verploegh: *Ztschr. f. physiol. Chem.*, lvii.

3. Mellanby: *Jour. Physiol.*, 1908, xxxvi, 447.

in connection with our subject, that Hoogenhuyze and Verploegh found that a professional faster, who had taken nothing but water for fourteen days, showed an increased creatinin excretion after exercise.

Cathcart<sup>4</sup> found that creatin is constantly present in the urine during starvation, and that carbohydrates given after fasting decrease the creatin output; whereas fat given after fasting increases the creatin excretion. He therefore puts forward the hypothesis that carbohydrates are absolutely essential for endocellular synthetic processes in connection with protein metabolism. This, of course, establishes a relationship between creatinuria and acetonuria as they are affected in a similar manner by the diet.

Studies of the creatinin excretion in children have been made by Hoffmann,<sup>5</sup> Rietschel,<sup>6</sup> Amberg and Morrill,<sup>7</sup> Amberg and Rowntree,<sup>8</sup> Funaro,<sup>9</sup> Sedgwick,<sup>10</sup> and Mellanby.<sup>11</sup> Work on the creatin excretion of children has been done by all but the first two.

In 1910<sup>10</sup> I discovered the fact that creatin, which has not been considered a normal<sup>12</sup> constituent of the urine of children, is excreted by the subjects of recurrent or periodic vomiting. At the St. Louis meeting of the A. M. A. I made the following statement:

"Thomas, a boy weighing 48 pounds, and a subject of cyclic vomiting, excreted on the fourth day, which was a hunger day, except for a few teaspoonfuls of a carbohydrate water, 49.9 mg. of creatin."

Evidently without knowledge of the above, and entirely independently, Mellanby,<sup>11</sup> of London, has confirmed my findings. He found creatin present in the urine of a boy of 6 years, both during two attacks and in

4. Cathcart: *Jour. Physiol.*, 1909, xxxix, 311. See also Benedict and Myers: *Am. Jour. Physiol.*, 1907, 362.

5. Hoffmann: *Virchows Arch. f. path. Anat.*, 1869, xlviii, 358.

6. Rietschel: *Jahrb. f. Kinderh.*, 1905, lxi, 615.

7. Amberg and Morrill: *Jour. Biol. Chem.*, 1907, iii, 311; *Jahrb. f. Kinderh.*, 1909, lxix, 280.

8. Amberg and Rowntree: *Bull. Johns Hopkins Hosp.*, xxi, No. 227, February, 1910.

9. Funaro: *Biochem. Ztschr.*, 1908, x, 467.

10. Sedgwick, *Jour. Am. Med. Assn.*, 1910, lv, 1178.

11. Mellanby: *Lancet*, London, 1911, clxxxi, 8.

12. Although it has been generally considered that creatin is not normally excreted after infancy, analyses by Rose, *Jour. Biol. Chem.*, 1911, x, 265, and the following determinations of my own throw some doubt upon this position:

Name	Age, Years	Condition	Creatinin in 100 c.c.	Creatin in 100 c.c.
Marie P. ....	8	Well	83	24.3
C. P. ....	6	Chronic cystitis	58	11.6
Harold K. ....	10	Chronic enteritis	46	11.6
S. S. ....	3	Well	47	8.1
A. S. ....	5	Well	96	18.5
J. S. ....	9	Well	64	7.0
H. N. ....	7	Well	122	9.3
C. P. ....	10	Chorea minor	88	23.2

the interim between them. He found also a marked rise of creatin excretion two or three days before the attacks.

My analyses are as follows:

CASE 1.—Thomas, aged 4, was seen first July 24, 1908, at which time he was having a typical attack of recurrent vomiting. He had the first attack when 2 years old. Attacks had usually been four or five months apart.

	Creatinin mg.	Creatin mg.
May 10, 1910, fourth day of attack, 6 years old....	.....	49.9
Sept. 11, 1911, well .....	379.8	251.5

The significant finding is that of the presence of creatin in the urine at two analyses over one year apart.

CASE 2.—Edward S., had his first attack during latter part of the first year. During the following year he had attacks at least every three weeks.

Date and Age	Creatinin mg.	Creatin mg.
Mch. 1909, 2 yrs. 10 mos., not vomiting. Wt. 12,270 gm. ....	193.	
Sept. 6, 1911. 4 yrs. 4 mos. Vomiting, fever .....	245.7	143.6
Sept. 7, 1911 .....	403.2	299.4
Sept. 23, 1911, well .....	215.6	48.4
Sept. 27, 1911, well .....	201.6	44.5
Sept. 30, 1911, fever, 102 F.; not vomiting.....	213.3	154.0
Oct. 5, 1911, 4 yrs. 5 mos.....	321.3	135.9
Oct. 7, 1911 .....	211.5	0.0
Oct. 10, 1911 .....	307.2	15.3
Oct. 16, 1911, Wt. 17,885 gm. ....	232.2	.....

In this case creatin was present between attacks, but was greatly increased during the attack as was the creatinin. September 30 the usual prodromata of an attack appeared, including fever, rhinitis, and rise in creatin, but the boy did not vomit.

CASE 3.—Orb. T., 10½ years old, has chorea and recurrent vomiting. She had an appendectomy at 9 years of age. She is under the care of Dr. Schlutz.

1911	Creatinin mg.	Creatin mg.
.....		
Sept. 6, not vomiting .....	389.4	34.1
Sept. 7, not vomiting .....	300.	0.
Sept. 13, not vomiting .....	462.	82.2
Sept. 30, not vomiting .....	198.4	66.7
Oct. 12, not vomiting .....	172.4	22.7

Here we have a child, not vomiting but excreting creatin.

CASE 4.—Stuart S., aged 6½ years, began to have attacks when 2 years old, occurring every month or six weeks. He has had no attacks since removal of the adenoids, February 25, 1909.

1911	Creatinin mg.	Creatin mg.
.....		
Sept. 12, well .....	250.8	122.4
Sept. 14, well .....	315.	52.1

In this case, one and a half years after the last attack, a large amount of creatin was being excreted.

CASE 5.—Jack T., 5½ years old, began to have attacks during his second year. In May, 1908, while under my care he vomited for fourteen days. The attacks are infrequent now and mild in character.

1911	Creatinin	Creatin
.....	mg.	mg.
Sept. 17, not vomiting .....	292.5	30.8
Sept. 18, not vomiting .....	378.	62.

In this case, although the attacks are much less frequent, creatin is excreted during the interval.

CASE 6.—Cecil W., 10 years old, began to have attacks during the second year. They were typical in character, in many of which I observed him, from the age of 2 to 9 years. In February, 1910, following an attack of appendicitis, the appendix was removed. He has had no attack since.

1911	Creatinin	Creatin
.....	mg.	mg.
Sept. 22, not vomiting .....	489.3	0.

CASE 7.—Leland W., 4 years old, is a brother of patient in Case 6. He had his first attack when 4 months old. Just before he was 3 years old he had very severe attacks. During 1910 he had five or six attacks. The adenoids were removed in February, 1911. He has had no attacks since. His mother says he has been absolutely well.

1911	Creatinin	Creatin
.....	mg.	mg.
Sept. 23, well .....	230.	47.2

Here we have creatin excreted over a half year after the last attack.

Other cases give similar results but mere repetition is hardly necessary. Attention is called to the fact that in Case 2 both the creatinin and creatin excretion reached a very high mark during the attack. These results show, as do Mellanby's,<sup>11</sup> that the creatin metabolism, that is, the endogenous nitrogen metabolism, is abnormal in recurrent vomiting, during the attacks.

#### B. ADENOIDS AND RECURRENT VOMITING

Many more or less unsatisfactory theories have been advanced concerning the etiology of recurrent or periodical vomiting. The well-known fact that acetone is present in the urine during the attacks has led to much discussion. Valgussa<sup>13</sup> wrote on the acid intoxication in these cases in 1901. Marfan<sup>14</sup> considered the acetonemia of importance. Pierson<sup>15</sup> wrote a year later on the subject of "Acetone and Diacetic Acid as a Cause of Persistent Recurrent Vomiting of Children." Then

13. Valgussa: Policlinico, Rome, 1901. Cited from Arch. de méd. des enf., 1901, iv, 681.

14. Marfan: Arch. de méd. des enf., 1901, iv, 841.

15. Pierson: Arch. Pediat., 1902, xx, 505.

Edsall,<sup>16</sup> in 1903, proposed that the acid intoxication, as he termed it, be treated with alkalis. Successful sodium bicarbonate therapy was reported by Albert Myers.<sup>17</sup> But Schrack<sup>18</sup> had shown in 1889 that starches given to a child with acetonuria relieve the condition. Hirschfeld<sup>19</sup> showed the fundamental relation between carbohydrate metabolism and acetonuria. Langstein and Meyer<sup>20</sup> definitely showed in 1905 that withdrawal of carbohydrates or hunger in children, produces acetonuria. The trend of opinion then began to turn and Morse<sup>21</sup> said in 1905 that the acid intoxication is presumably always secondary. Edsall<sup>22</sup> voiced a similar opinion in discussing Howland and Richard's paper in 1907. Shaw and Tribe<sup>23</sup> stated in 1905 that "some cases of recurrent vomiting are quite different from others in that they fail to respond to treatment with massive doses of alkalis." Janeway and Mosenthal<sup>24</sup> believe that too little attention is paid to the factor of carbohydrate starvation in the reports of recurrent vomiting. Mellanby<sup>25</sup> finally clinched the matter by withdrawing the carbohydrates from the diet of a subject of recurrent vomiting, at the time apparently well, causing acetonuria without producing an attack, he then overcame the acidosis by giving glucose. He says: "This is conclusive proof that acidosis in itself had nothing whatever to do with the symptoms of cyclic vomiting. To apply the term 'acid intoxication' to such a condition would then be absolutely wrong and misleading."

Post-mortem examinations have shed little light, unless the fatty degeneration of the liver reported by Jones,<sup>26</sup> and the suprarenal hemorrhage in Langmead's<sup>27</sup> case are significant.

Comby<sup>28</sup> considers appendicitis, which was present in nearly 50 per cent. of his cases, to be of importance. In my series of twenty-two cases, seven had symptoms of appendicitis and two were operated on with cessation of the attacks. Mucomembranous enteritis is insisted on by Ausset<sup>29</sup> as bearing a relation to recurrent vomiting.

16. Edsall: *Am. Jour. Med. Sc.*, 1903, cxxv, 629.

17. Myers: *Arch. Pediat.*, 1906, xxiii, 530.

18. Schrack: *Jahrb. f. Kinderh.*, 1889, xxix, 411.

19. Hirschfeld: Cited from *Handb. d. Path. des Stoffwechsels*, Noorden, i, 182, Hirschwald, Berlin, 1906.

20. Langstein and Meyer: *Jahrb. f. Kinderh.*, 1905, lxi, 454.

21. Morse: *Arch. Pediat.*, 1905, xxii, 571.

22. Edsall: *Arch. Pediat.*, 1907, xxiv, 401.

23. Shaw and Tribe: *Brit. Med. Jour.*, 1905, i, 349.

24. Janeway and Mosenthal: *Arch. Int. Med.*, 1908, ii, 214.

25. Mellanby: *Lancet*, London, 1911, clxxxi, 8.

26. Jones: *Arch. Pediat.*, 1909, xxvi, 446.

27. Langmead: *Brit. Med. Jour.*, 1905, i, 352.

28. Comby: *Arch. de méd. des enf.*, 1905, vii, 741.

29. Ausset: *Arch. de méd. des enf.*, 1906, ix, 767.

Ely<sup>30</sup> believes recurrent vomiting is a "distinct neurosis," and Fischl<sup>31</sup> thinks the attacks may be hysterical in nature. Nauwelaers<sup>32</sup> considers the condition under arthritism. Howland and Richards<sup>33</sup> believe it due to diminished oxidation. Irving Snow<sup>34</sup> states that the vomiting is "sometimes due to a sudden hypersecretion of irritating gastric juice." Richardiere<sup>35</sup> considers the liver of primary importance and Saunders<sup>36</sup> speaks of "hepatic insufficiency." Hecker<sup>37</sup> believes that the condition is fundamentally a disturbance of the fat catabolism. And finally Mellanby<sup>38</sup> suggests that the condition of recurrent vomiting is due to some intestinal intoxication which may or may not depend on bacteria, and may depend on an accumulation or excessive formation of beta-imminazol-ethylamine in the intestinal wall.

Before such an array of diverse opinions, it is with considerable trepidation that I mention the long-suffering subject of adenoids. After citing the literature bearing on the subject, I shall therefore state briefly my clinical observations, and not stand sponsor for any fine-spun theories.

Averagnet<sup>38</sup> observed vomiting and diarrhea, as well as enteritis with mucomembranous stools, in children with coryza, pharyngitis and hypertrophied tonsils, and he saw these conditions cured by caring for the rhinopharyngitis. Breton<sup>39</sup> reports a case of daily vomiting, with mucomembranous stools, cured by removal of the adenoids. Now turning to recurrent vomiting proper, Comby<sup>28</sup> mentions adenoids in 18 per cent. of his cases. Griffith<sup>40</sup> noted sore throat accompanying the attacks. Misch<sup>41</sup> reports that the angina which accompanies the attacks is as a rule a catarrhal inflammation. One of Irving Snow's<sup>32</sup> patients had an attack following hoarseness, nasal discharge and fever. Rachford<sup>42</sup> says: "Recently I have been especially interested in vasomotor coryza as an almost constant warning symptom in a number of cases." Sagher saw a child 6 years old that had eczema in its second year, which, after the removal of the adenoids, had no more attacks "in spite of the fact that the diet was enriched."

30. Ely: Jour. Am. Med. Assn., 1903, xl, 846.

31. Fischl: Handbuch d. Kinderheilk., ii, 163, Vogel, Leipzig.

32. Nauwelaers: La Clinique, 1903, No. 18. Cited from Monatschr. f. Kinderh., 1903, ii, 251.

33. Howland and Richards: Arch. Pediat., 1907, xxiv, 401.

34. Snow: Am. Jour. Med. Sc., 1904, cxxviii, 966.

35. Richardiere: La Clin. Infant., 1905, Cited from Jahrb. f. Kinderh., lxi, 804.

36. Saunders: Arch. Pediat., 1908, xxv, 104.

37. Hecker: Ergebn. der inn. Med. u. Kinderh., 1911, vii, 242.

38. Averagnet: Soc. de pediat., Nov. 14, 1899, reported in Arch. de méd. des enf., 1899, ii, 767.

39. Breton: Rev. mens. d. mal. de l'enf., 1900, xviii, 235.

40. Griffith: Am. Jour. Med. Sc., 1900, cxx, 553.

41. Misch: Jahrb. f. Kinderh., 1905, lxi, 533.

42. Rachford: Neurotic Diseases of Childhood, p. 220, 1905, E. B. Treat & Co., New York.



Janeway and Mosenthal<sup>24</sup> state, referring to recurrent vomiting: "The strongest argument in favor of its being due to an undiscovered focus of infection is the leukocytosis."

Of my series of twenty-two cases, twenty patients had adenoids or enlarged tonsils. Most of them had fever before or during the attacks. The posterior cervical glands were usually enlarged. A very common prodrome of the attacks was sore throat or nasal discharge. One "had bleeding nose at the times of the attacks." Chorea minor, rheumatism and endocarditis were complications in three cases. Geographical tongue and asthma were noted. But the observation which warrants this presentation is the surprising result of removal of the adenoids in some of these cases.

CASE 1.—Leland W., 4 years old, had classical, frequent, recurrent vomiting from the latter half of his first year. Tonsillitis was a usual prodrome of the attacks. The tonsils and adenoids were removed in February, 1911. The mother stated on Sept. 21, 1911, that the child had been "perfectly well since."

CASE 2.—Cecil W., 10 years old, a brother of patient of Case 1, had typical attacks from his second year. The adenoids were removed when he was 6 years old. He had no more attacks for a year. He had two light attacks during the eighth year. Then he developed appendicitis, and has been perfectly well since his appendix was removed in February, 1911.

CASE 3.—Stuart S., 6½ years old, began to have recurrent vomiting attacks with high fever and rhinopharyngitis in his second year. The attacks occurred every month or six weeks. They were becoming more frequent. On Feb. 25, 1909, his adenoids were removed. There have been no more attacks from that date to the present, October, 1911.

CASE 4.—Edward S., 5½ years old, began to have recurrent vomiting attacks during his first year and had vomiting periods at least every three or four weeks until the adenoids were removed in the Fall of 1908. For six months after the operation he was free from attacks; then he had occasional lighter attacks. During the past six months these have been more frequent but lighter. At the same time, however, it is to be noted that the boy has begun to have a great deal of rhinitis again. The father, who is a rhinologist, considers the condition similar to hay fever. The mother, who is a trained nurse and a careful observer, states that she has always noticed that he has "a head cold and a cough preceding the spells."

CASE 5.—Thomas A., 7 years old, gives a history very similar to that of Case 4; that is, comparative freedom from attacks for months after the operation, with recurring attacks on return of the rhinopharyngeal trouble. In this case the nasopharyngeal disturbance caused by the operation was followed immediately by a typical and severe run of vomiting.

CASE 6.—Bernice S., 11 years old, was first seen in 1906 with recurrent vomiting. Rhinopharyngitis always accompanied the attacks. The attacks did not cease at once after removal of the adenoids, but became gradually lighter and less frequent. She has had no attacks for several years.

CASE 7.—H. W. In this case the operation was imperfectly performed, and the attacks, though lighter, still recur.

CASE 8.—Louisa, 4 years old, has had periodic vomiting attacks since early in the first year. The adenoids were removed in October, 1910. The mother reports, Oct. 13, 1911, that she has only had two attacks since the operation that have been at all serious, so that the number of attacks is only half that of the previous year.

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THE ETIOLOGY AND TREATMENT OF THE SO-CALLED  
HEMORRHAGIC DISEASE OF THE NEW-  
BORN: WITH REPORT OF CASES

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**NEW YORK    BROOKLYN**

## I. INTRODUCTION

In spite of a vast literature our knowledge of the causation of hemorrhage in the new-born is incomplete. The clinical picture varies widely in different cases. The lesions revealed by post-mortem examination are inconstant. Bleeding from the skin, the umbilical cord, the mucous membranes or the viscera—either singly or combined—is the only feature common to all cases.

In addition to the general disease which may be the underlying factor in the production of hemorrhage, the ultimate cause of all persistent and uncontrollable bleeding is probably a blood or vascular change. It seems only rational to suppose that the initial bleeding is induced by a vascular lesion. The cause for the persistent hemorrhage is to be sought in some defect of the normal mechanism for the control of bleeding—the clotting of the blood.

It is with this phase of the etiology of hemorrhage in the new-born that our present communication is essentially concerned.

## II. REPORT OF CASES

CASE 1.—Sudden onset of intestinal hemorrhage in an apparently normal infant fifty hours old. Death in two hours and fifty minutes. Imperfect coagulation of the blood due apparently to a deficiency of fibrinogen.

*History.*—Baby G., a female infant, was born at the Nursery and Child's Hospital Feb. 11, 1911, at 2 a. m. The family history was unimportant. Labor was normal. The patient was the first child. The mother received about 15 c.c. of chloroform during the third stage of labor. The birth-weight was 7 pounds 6 ounces; the infant was well developed and seemed normal in every way during the first two days.

On the third day (February 13), at 4:30 a. m., without premonitory symptoms, there was a profuse intestinal hemorrhage. The blood was dark and partially coagulated. During the next two hours a number of similar hemorrhages occurred at varying intervals. The infant became pallid, the skin dry and wrinkled, the pulse rapid and weak. These symptoms became exaggerated with each hemorrhage. Death occurred at 6:45 a. m. No treatment was used beyond the external application of heat and the administration of epinephrin solution by mouth.

*Examination of the Blood.*—A post-mortem examination was not allowed but permission was given to obtain blood by aspiration of blood vessels. At 9:30 a. m., 2½ hours after death, about 60 c.c. of blood was obtained from the lateral

and longitudinal sinuses and the femoral vessels. Cultures were made on agar, bouillon and blood serum. The media remained sterile. A Wassermann test was negative. The remaining blood was divided into two portions of about 25 c.c. each, to one of which was added 1/10 volume of a 1 per cent. ammonium oxalate solution.

The unoxalated blood showed no evidence of coagulation in 10 minutes; when examined thirty-five minutes later, partial coagulation had occurred. The clot was soft, loose meshed and gelatinous. This blood was in two separate vessels. That in one vessel was allowed to stand undisturbed for two hours, at which time no further coagulation had occurred. The clot had retracted slightly from the sides of the vessel but was still soft and gelatinous and did not affect all of the blood. On slight agitation the clot was disintegrated completely; the blood was then perfectly fluid and with the exception of the presence of a few fibrin flocculi, it resembled ordinary unclotted blood.

The unoxalated blood in the remaining vessels was used for the following experiments:<sup>1</sup>

1. The addition of 0.1 c.c. of a 1 per cent. solution of calcium chlorid to 3 c.c. of the partially clotted blood was without effect. The further addition of calcium chlorid did not affect the nature of the clot.

2. To 3 c.c. of the blood was added defibrinated normal human blood in portions of 0.1 c.c. each. No further coagulation occurred even after the addition of 1 c.c. of the defibrinated blood.

3. The addition of a drop of normal human blood to 2 c.c. of the infant's blood plasma was without effect. The normal blood coagulated; the infant's blood was unchanged.

4. The infant's blood diluted and in full strength exerted no perceptible inhibiting influence on the coagulation of normal blood.

The oxalated blood remained fluid and was used for the following experiments:

1. The addition of a 1 per cent. solution of calcium chlorid solution produced coagulation within three minutes. Coagulation was incomplete and the clot presented the same characteristics as that which formed spontaneously in the unoxalated blood. The addition of varying amounts of calcium chlorid was without influence on the nature of the clot.

2. The same sort of incomplete coagulum was formed when the oxalated blood was treated with defibrinated blood in addition to calcium chlorid.

3. The oxalated blood exerted no inhibiting influence on the coagulation of normal blood. (After the addition of calcium chlorid.)

The presence of thrombin in the infant's blood was further shown by the following experiment:

Twelve c.c. of the partially coagulated blood was used for the extraction of thrombin by Schmidt's method. The blood was allowed to stand under alcohol for three months. The precipitate was collected on a small filter, dried over sulphuric acid, and extracted with about 4 c.c. of water. A few drops of the aqueous extract was sufficient to produce coagulation of a solution of fibrinogen. The fibrinogen was freshly prepared from dog's blood plasma by half saturating with sodium chlorid. It was purified in the usual manner and did not coagulate spontaneously or on the addition of sodium or calcium chlorid.

1. All of the experiments were made in duplicate and controls of normal blood were used for comparison. Normal saline solution was added to the controls in sufficient quantity to produce the same dilution as in the actual experiments. All experiments were made at room temperature (21 degrees C.).

At the conclusion of each experiment the clot was disintegrated by agitation of the vessel. In each instance only slight agitation was required to render the blood perfectly fluid. The amount of fibrin was extremely small and consisted only of a few flocculi.

#### DISCUSSION

The exact coagulation time of the blood in this case is uncertain, but it was probably prolonged since coagulation had not taken place at the end of ten minutes though it had occurred at the end of forty-five minutes. The presence of all of the blood elements essential to coagulation was shown by the spontaneous occurrence of clotting. Coagulation, however, was incomplete and the resulting clot soft and fragile. Such a condition might be due to a deficiency of thrombin, of calcium, of fibrinogen, or to the presence of some agent which exerts an inhibiting action on clot formation. That the impaired coagulation in this case was not due to a deficiency of calcium or thrombin is indicated by the fact that the addition of these substances did not render coagulation more complete. Moreover, the presence of an excess of thrombin was shown directly by the Schmidt method. It seems improbable that an inhibiting substance (antithrombin) was responsible for the condition, as the infant's food <sup>6'000</sup> did not interfere with the coagulation of normal blood.

Although the quantity of fibrin formed was not determined quantitatively, yet the amount was extremely small and was unquestionably below the normal. Moreover, the quantity of fibrin was not increased by the addition of calcium or thrombin. It seems, therefore, that the impaired coagulation of the infant's blood was due to a deficiency of fibrinogen or perhaps to some change in that substance through which it was rendered uncoagulable.<sup>2</sup>

It is unfortunate that a post-mortem examination could not be obtained in order to determine, if possible, the initial cause of the hemorrhage. There was no clinical evidence of infection and a blood culture was negative. There was no family history of syphilis and the absence of this disease was indicated by the negative Wassermann test.

In many similar cases no pronounced pathologic changes have been demonstrated, in other cases the intestinal mucosa has shown varying degrees of acute congestion, while in a third group of cases, ulceration of the gastro-intestinal mucosa has been the apparent origin of the hemorrhage.

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2. Whipple and Hurwitz (Fibrinogen of the Blood as Influenced by the Liver Necrosis of Chloroform Poisoning. *Jour. Exper. Med.*, 1911, xiii, 136) observed that a tendency to hemorrhage due to a deficiency of fibrinogen was caused in dogs by chloroform necrosis of the liver. It is impossible to determine whether the small amount of chloroform given to the mother of this patient was a factor in the causation of the bleeding.

**CASE 2.**—*Slightly prolonged labor. Instrumental delivery. Abrasion of the mucous membrane of the lip and subcutaneous hemorrhage on the nose. Hemorrhage from the nose and mouth twenty-four hours after birth. Hematemesis. Purpura. Subcutaneous injections of blood from the father; recovery.*

**History.**—Baby F., a male infant, was born March 2, 1911, at the Samaritan Hospital in Brooklyn. The family history was irrelevant. There were no previous children.

Labor was prolonged and the baby was delivered by a median forceps operation. The mother was anesthetized for forty-five minutes (mixed chloroform and ether).

The infant was slightly asphyxiated and about fifteen minutes was required for complete resuscitation. There was an abrasion of the upper lip and a subcutaneous hemorrhage on the nose. The infant weighed  $7\frac{1}{2}$  pounds.

Beyond the birth injuries above noted there was nothing abnormal during the first twenty-four hours. On the morning of March 3, blood began to ooze from the nose and mouth. A small amount of blood was vomited during the afternoon. The hemorrhage was controlled temporarily by the application of 1 to 1,000 epinephrin solution, but in each instance it would recur within a short time. The abrasion on the lip was sutured but this measure only gave rise to additional hemorrhage.

**Examination.**—The bleeding continued and on March 4, the baby was weak and apathetic and made no attempt to nurse. Examination at this time disclosed a subcutaneous ecchymosis on the tip of the nose and a series of purpuric spots on the neck and back which extended from the base of the skull to the sacrum. The individual spots varied from 1 to 3 cm. in diameter. There was a purpuric spot about 1 cm. in diameter on the right ankle and two of similar size on the left leg. There were abraded surfaces on both lips from which blood continually oozed. The skin and conjunctivæ showed a pronounced degree of jaundice. The skin was drawn, the cry feeble and the general condition seemed worse than would be accounted for by the loss of blood.

**Treatment.**—At 3:15 p. m., March 4, 7 c.c. of blood obtained from the father was injected into the subcutaneous tissue of the infant's back. By 5:15 p. m. the blood was absorbed entirely and the puncture wound alone marked the site of injection. At 10 p. m. the hemorrhage had not ceased and a second injection of 16 c.c. of the father's blood was given. This blood was absorbed within two and one-half hours. The hemorrhage decreased but did not cease entirely; there was still a slight oozing of blood from the nose and mouth and during the night a small amount of blood was vomited. At 12 m., March 5, a third injection of 24 c.c. of blood was given. Absorption occurred within four hours. During the afternoon the bleeding decreased and by midnight had ceased.

Improvement was continuous from this time and on March 18, when 16 days old, the infant appeared entirely normal for its age. Beyond the external application of heat, no other treatment was used.

**Examination of the Blood.**—On March 4, the coagulation time of the infant's blood was twenty minutes, that of a normal adult used as a control, six minutes (Hinman and Sladen's method). Only about 3 drops of blood escaped from the puncture wound and within six minutes a firm, well-retracted clot had formed over its surface. A second puncture was made in the soft tissues of the heel from which about 2 c.c. of blood was obtained for a Wassermann test. A drop of blood obtained from this wound did not coagulate within twenty-five minutes. The addition of a trace of defibrinated normal blood caused immediate coagulation. The bleeding from this wound was rather scant and it was only by means of considerable pressure that sufficient blood was obtained. A firm clot formed over the surface of the wound within a few minutes.

The blood obtained for the Wassermann test began to coagulate in about twenty minutes and at the end of an hour a tough coagulum had formed. The Wassermann test was negative.

## DISCUSSION

The investigation of the blood of this patient presents several points of interest. As determined by ordinary clinical methods, coagulation was delayed, and was accelerated by the addition of defibrinated blood. It seems improbable, however, that the hemorrhage in this case was due entirely to a general hemorrhagic diathesis, for there was no continued bleeding from injuries of normal tissues (skin punctures). The hemorrhage occurred from primary local injuries to the tissues of the nose and mouth and it seems only rational to assume that there was some condition in these areas due to which normal clot formation and arrest of hemorrhage did not occur.

The fact that the coagulation of the blood was delayed and was accelerated by the addition of thrombin and thrombokinase (defibrinated blood) indicated that there was a defective action of one or both of these substances. The absence of continued bleeding from injuries of normal tissue suggests that the blood defect was corrected by some substance supplied by the injured cells (kinase?). Moreover, it seems possible that a lack of this substance in the injured areas of the nose and mouth was responsible for the continued hemorrhage.

The cause of the purpuric spots in this case is obscure and has relation to the general pathology of the disease. It seems improbable that syphilis was a causative factor since both the family history and a Wassermann test were negative. Bacterial infection cannot be excluded as no blood culture was made. If such was the origin of the disease, the purpuric manifestations could be explained by the occurrence of emboli or by injuries to the vessel wall. The absence of fever, however, during the entire illness is not in accord with bacterial infection; at least, not of the ordinary septic type.

The marked jaundice in this case, and the pronounced asphyxia at birth, taken in connection with the prolonged anesthesia of the mother, suggests that a toxic action of the chloroform was perhaps a factor in the causation of the disease. But we have no direct evidence which would serve to elucidate this question.

**CASE 3.**—*Operative delivery. Hemorrhage into subcutaneous tissues. Bleeding from the umbilical cord. Normal coagulation of the blood. Subcutaneous injections of blood from the parents. Death on the sixth day.*

**History.**—Baby K., male, born April 2, 1911. The patient was born at term and was the fifth child. The second child died at the age of 5 days from a disease associated with hemorrhages into the skin. The family history was otherwise irrelevant.

The baby was well developed at birth and weighed  $7\frac{1}{2}$  pounds. Delivery was by podalic version. The mother was anesthetized with chloroform. The infant appeared healthy, took the breast eagerly and slept well. On April 3, the attending physician noted a small extravasation of blood over the external surface of the left ankle.

On April 5, the infant seemed quite ill, was restless and refused the breast. The pulse was rapid (140) and the respirations increased in frequency. The rectal temperature was 98 F. the extravasation of blood on the left ankle had spread considerably and an additional hemorrhage was noted over the right ankle. There was also an extravasation of blood in the region of the right buttock. These hemorrhages had appeared during the night.

At 1 p. m. the patient was seen by Dr. Commiskey and 10 c.c. of blood from the mother was injected into the subcutaneous tissue of the back. At 8 p. m. a small subcutaneous hemorrhage had appeared in the right upper eyelid. The hemorrhagic area on the buttock had spread toward the external surface of the thigh. The respirations were increased in frequency (38 to the minute), the pulse was 150 and the temperature 97 F. The patient was extremely pallid and at this time there was oozing of blood from the umbilical cord.

On the morning of April 6, the infant seemed worse. The hemorrhagic areas, with the exception of the one on the right eyelid, had spread considerably. A new subcutaneous hemorrhage had appeared near the angle of the left scapula. Ten c.c. of blood from the father was given by subcutaneous injection. The patient showed no improvement and died rather suddenly at 3 p. m.

The temperature remained subnormal throughout the entire illness. Physical examination disclosed nothing of importance beyond the signs noted.

*Examination of the Blood.*—On April 5, the coagulation time of the infant's blood was five minutes (Hinman and Sladen's modification of the method of Milian). Coagulation was complete with normal retraction of the clot. Blood obtained for a Wassermann reaction began to coagulate within a few minutes and at the end of fifteen minutes showed the presence of a well formed clot. On April 6, the coagulation time was also five minutes. The punctures of the skin gave rise to only slight bleeding, and clot formation over the injured area was normal in every way.

#### DISCUSSION

This case differs considerably from the others inasmuch as the external hemorrhage was very small and was represented only by a slight oozing of blood from the umbilical cord.

If the term "hemorrhagic disease" is restricted to those cases in which the loss of blood is sufficient to account for the symptoms, it is somewhat questionable whether this case should be included, since the external hemorrhage was slight. In many cases, however, with slight external hemorrhage, and in a few cases in which there was no evidence of hemorrhage during life, the post-mortem examination has shown extensive hemorrhage into the internal organs. As a matter of fact, some degree of internal hemorrhage occurs in many cases of the so-called hemorrhagic disease of the new-born.

Whether the symptoms and the fatal termination of the disease in this case were due to internal hemorrhage, or whether some general disease was the direct cause and the hemorrhage only a minor manifestation, cannot be determined, as a post-mortem examination was not obtained.

The direct cause of the disease is therefore equally uncertain. The negative family history and a negative Wassermann test seem sufficient to exclude syphilis as a causative factor. There was no evidence to indicate that the disease was due to bacterial infection, for the temperature

was subnormal throughout the entire illness and none of the symptoms usually present in bacterial infection were observed. Yet an infectious origin cannot be excluded with certainty, since it was impossible to obtain a blood culture.

The blood examination throws no light on the cause of the hemorrhage. Coagulation occurred within the normal time and clot formation was complete. It seems improbable, therefore, that the hemorrhage was dependent on a general defect of the blood. It is possible, however, that the hemorrhagic manifestations were due to localized vascular lesions.

### III. GENERAL DISCUSSION

#### ETIOLOGY

We have investigated the coagulation of the blood in ten cases of the so-called hemorrhagic disease of the new-born. The results are given in the accompanying table.

TABLE SHOWING COAGULATION TIME OF BLOOD IN THE AUTHOR'S TEN CASES

Case	—Coagulation Time, Minutes—		Bleeding from Skin Punctures
	During Hemorrhage	After Recovery	
1*	+90	4	+
2	+30	3-4	+
3	9	8½	—
4	5¾	7	+
5	9	3¾	+
6	3½	†	—
7	6	†	—
8	Between 10 and 45	†	..
9	20	5	—
10	5	†	—

\*Cases 1 to 7, inclusive, were reported in our paper on Spontaneous Hemorrhage in the New-Born, *AM. JOUR. DIS. CHILD.*, 1911, i, 276. Cases 8, 9 and 10 are included in this paper. †Died.

In four cases the coagulation time was practically normal, in two cases coagulation was slightly delayed, in two cases there was a decided delay, while in two cases coagulation was greatly delayed or absent.

These observations do not show that all cases of hemorrhage in the new-born are dependent on a general hemorrhagic diathesis. On the basis of the blood examinations the cases may be divided into at least two groups. In one group of cases the uncontrollable hemorrhage is apparently dependent on defective blood coagulation. The coagulation time is prolonged to a greater or lesser degree and there is a tendency to continued bleeding from punctures of the skin. In this group belong Cases 1 and 2 in which the coagulation of the blood was greatly delayed or absent and in which considerable bleeding was caused by skin punctures. In both cases there was an apparent defect in the action of thrombin. Similarly in Case 8, the onset of coagulation was delayed



and clot formation was incomplete. In this case there was apparently a deficiency of fibrinogen. In the presence of a primary injury to the vessels these blood defects are sufficient to explain the persistent hemorrhage.

In the second group of cases the coagulation time of the blood is slightly if at all prolonged and there is no tendency to hemorrhage from skin injuries. A different explanation must be sought for the hemorrhage in these cases.

Hemorrhagic conditions of this type have been attributed by some observers to defective retraction of the clot, due possibly to a deficiency of blood platelets. It is easily conceivable that coagulation may occur as quickly as normal, but with the formation of a loose meshed clot which is not of sufficient firmness to control the bleeding. That some cases of uncontrollable hemorrhage in the new-born may be dependent on this condition is possible, although we are aware of no direct observations to show that such is the case.

In two of our cases, however (4 and 5), although the coagulation time was normal, persistent hemorrhage occurred from punctures of the skin. It is possible that the hemorrhage in these cases was due to a deficiency of some substance essential to proper retraction of the clot.

Defective clot retraction, however, cannot be the cause of the hemorrhage in all cases with normal coagulation time of the blood. There are some cases of hemorrhage in the new-born in which blood coagulation not only occurs within the normal time but is also complete. In three cases observed by us the coagulation time was normal and there was no abnormal bleeding from punctures of the skin, the bleeding from which was quickly controlled by the formation of a firm, well-retracted clot. These observations indicate that the hemorrhage was not dependent on a generalized blood or vascular lesion, but rather on some localized condition present only in the areas from which the hemorrhage occurred. It seems probable that the bleeding was due to a localized vascular lesion.

The relationship of the vessels to the control of bleeding is one of great importance but is not well understood. Hemorrhages in the nature of purpura and ecchymoses are probably dependent on localized vascular lesions which may be due to infective emboli, or which may be of purely toxic origin.

An injury to the vessel wall leads to the occurrence of a thrombus which controls the bleeding. The formation of the thrombus commences on the injured surface of the vessel wall and is probably induced by some substance which is liberated or produced by the injury. It has been found that a substance (thrombokinas<sup>2</sup>) can be obtained from the vessels

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2. Bernheimer: The Reaction of the Vessel Wall to the Coagulation of the Blood, *Jour. Am. Med. Assn.*, 1910, *lv*, 283.

which is of influence on blood coagulation and it is not improbable that its action is essential to the proper control of bleeding. A local absence or interference with the production or action of this substance, due to infection, a congenital defect or injury, is perhaps the cause of the localized type of hemorrhage in which the coagulation of the blood, as determined by ordinary clinical methods, is entirely normal.

The attempt to determine the pathology of the blood in hemorrhagic conditions is beset with numerous obstacles. Not the least of these is due to the fact that a number of the phases of normal blood clotting are imperfectly understood. It is improbable, therefore, that the exact causation of hemorrhage in the new-born can be definitely ascertained until the physiologic process is more thoroughly known.

From the data at our disposal, however, it seems clear that we can scarcely expect to find that all cases of hemorrhage in the new-born are dependent on the same cause. The inconstant clinical picture, the different pathologic conditions with which these hemorrhages are associated, and the variations found in the blood coagulability, all serve to indicate that a number of different pathologic conditions giving rise to hemorrhage have been classed together as the "hemorrhagic disease of the new-born."

#### TREATMENT

The various measures used in the treatment of hemorrhage in the new-born have been discussed in a previous paper.<sup>1</sup> We have treated nine of these patients by means of the subcutaneous injection of whole blood. This procedure is simple, perfectly harmless, and so far as can be judged from a small series of cases, efficacious. The harmlessness of the procedure and its apparent efficacy is shown in Case 2. The injected blood was quickly absorbed and was apparently without harmful influence on the patient. Case 3, however, which was treated in the same way, terminated fatally, but in this case there was practically no external bleeding and it is impossible to determine whether the fatal outcome was due to hemorrhage or to some other cause. Case 6 (former series) also terminated fatally. This patient was in a moribund condition at the time treatment was instituted and died three and a half hours after admission to the hospital.

In our earlier cases we used smaller amounts of blood at less frequent intervals than in Case 2. From our experience in this case we believe that the best results can be obtained from the injection of 10 to 30 c.c. of blood, the injection to be repeated every four to eight hours as long as the hemorrhage continues.

It can scarcely be expected that such a therapeutic measure will prove a cure for all cases. There are apparently a number of different condi-

tions which may be responsible for hemorrhage in the new-born, and there is no indication that the pathologic condition of the blood is always the same.

In the cases in which the hemorrhage is profuse and which are as a rule quickly fatal (Case 1), it seems scarcely possible that any of the simpler measures could be of value. In the treatment of such cases an immediate transfusion of human blood is probably the only means from which any result could be expected.

#### IV. SUMMARY AND CONCLUSIONS

1. In the hemorrhagic conditions of the new-born, the coagulation of the blood may be normal, delayed or absent.

2. A deficiency or absence of thrombin or fibrinogen may give rise to imperfect blood coagulation and uncontrollable hemorrhage.

3. In some cases of hemorrhage in the new-born in which blood coagulation is apparently normal, it seems probable that the hemorrhage is due to some localized vascular lesion or defect present only in the areas from which the bleeding occurs.

4. The subcutaneous injection of whole blood is harmless and is of apparent value in the treatment of the hemorrhage.

We take great pleasure in acknowledging our indebtedness to Dr. Thomas S. Southworth for the privilege of observing Case 1. Our thanks are due to Dr. O. P. Humpstons and Dr. Donald McNaughton for their kindness in permitting us to report Case 2, and to Dr. J. Bernstein for the notes on Case 3. We are indebted to Dr. F. Gett, Dr. C. Schredick and Dr. F. G. Schaible for the Wassermann tests.

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## RECENT DEVELOPMENTS IN PASTEURIZATION OF MILK FOR A GENERAL MARKET \*

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Pasteurized milk, according to the definition of the Secretary of Agriculture, is milk that has been heated below the boiling point, but sufficiently to kill most of the active organisms present, and immediately cooled to 50 F. or lower. The process of pasteurization as we know it to-day is employed either to prevent communication of disease through milk to the consumer or to avoid "disease of milk." The process was first worked out by Pasteur to preserve wine and beer and had no reference to diseases of man. Soxhlet in 1886 devised tubes and methods for sterilizing milk so that it would keep. These methods were introduced into the United States by Caillé<sup>1</sup> in 1888, who, in an article on the subject, states that some thirteen years before Jacobi had recommended sterilization of milk. These methods all had as their object the preservation of milk and it was not until later that real pasteurization was employed to kill pathogenic organisms. The purposes of pasteurization may now be regarded as legitimate or fraudulent. The legitimate objects are to destroy pathogenic bacteria and to preserve milk so that it may be transported, when properly refrigerated, to localities where fresh milk is not obtainable. The fraudulent uses are designed to give a low bacterial count to carelessly handled and stored dirty milk, a redemption process, and to make milk keep in a manner similar to that of carefully obtained clean milk. In any event the process depends on heating milk for a sufficient period of time so that the offending micro-organisms will be disposed of. When pasteurization is resorted to to redeem milk it is only essential that a large percentage of bacteria be destroyed, while if milk is to be rendered free from the possibility of causing infection it is imperative that all non-spore-bearing pathogenic organisms be killed. Unfortunately not all pasteurization of milk is done for a legitimate purpose and therefore "pasteurization of milk" must suffer through offenders, and offenders can get a trade advantage as well

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\*Milk research fellowship established and supported by the Milk and Baby Hygiene Association of Boston.

1. Caillé: Report of some experiments made to determine the proper manner of boiling and preserving milk for the use of infants, New York, 1888.

as those who employ the process for legitimate purposes. The label "Pasteurized Milk" means little to-day unless the kind of milk pasteurized and the time and temperature of heating is stated and all is done under official supervision. Nor is supervision by an "expert" enough, for experts are easily found and many of them are incompetent or biased.

Pasteurization depends for its efficiency on heating to or beyond the thermal death-point of pathogenic bacteria. To do this milk is exposed momentarily to a temperature of about 170 F. or to 140 to 150 F. for from twenty to sixty minutes. The first method is called the "flash" method and "commercial method" by some, while the latter method is called the "holding" method. Both methods are supposedly based on data derived from the laboratory. Laboratory methods, however, are not sufficient. In the laboratory small portions of milk are heated in test-tubes and bottles while in the trade large amounts of milk must be pasteurized. Furthermore, bottles for the market must be filled to the top when cold which makes pasteurization in the paper stoppered bottle impossible. To overcome this difficulty means have been devised to heat milk in bulk before cooling and bottling. This, however, makes reinfection, not only with saprophytic, but also with pathogenic organisms, possible.

This reinfection can largely be done away with by sterilization of the cooler, bottle filler, caps and bottles. Capping machines which are claimed to make handling unnecessary are used almost universally. Due to mechanical defects and pressure for time for pasteurization, cooling, bottling and capping, pasteurization in the bulk is not as reliable nor as consistent as might be hoped for. If reinfection can occur it is only fair to suppose that infection with pathogenic organisms can also occur. It is argued that this has never been the case and that no epidemic has followed the consumption of pasteurized milk. Whether this is true or only apparent, is an open question. A number of instances have been reported in which individuals capable of transmitting infection have come in contact with pasteurized milk before the process of bottling and capping was completed. Pasteurization has been advanced as a panacea but probably diseases which may have been transmitted through pasteurized milk have not been referred to it simply because the milk consumed had been "pasteurized." Fortunately during the past year tin caps with a cork lining such as are used for capping beer bottles have been adapted to milk bottles and when these are used it is possible to pasteurize milk in sealed packages. Various mechanical devices for immersing milk bottles in heated water or subjecting them to a spray of the desired temperature are now available.

All of the methods and devices for pasteurizing milk have defects or are expensive. For pasteurization in bulk, milk is rapidly heated by

forcing a thin stream of milk over a surface heated by steam or hot water. This heating surface is much higher in temperature than that to which the bulk of milk is heated and therefore it is evident that a part of the milk is also heated much above the desired temperature. When hot water is used for heating milk the temperature of the heating surface does not fluctuate as much as when steam is used. Employment of the holding device adds further difficulty. When milk is held in rotating sectional tanks the time in which one complete circuit is made is not necessarily the same as the time for which milk is held, for if the last milk emptied into a tank just before it is filled is of slightly lower temperature than that already in the tank the cooler milk will fall to the bottom and therefore be the first to run out of the tank. Thus, if it requires twenty minutes for one revolution of a four compartment tank, underheated milk will leave the tank after being held only fifteen minutes. In all holding devices currents caused by hotter or colder milk are very important and are probably best overcome when a number of Park's tanks are connected in series. Foam collecting on the top of tanks is of lower temperature than the milk and therefore in it pasteurization may not be efficient. The various devices for warming cold milk over surfaces heated by hot milk and at the same time cooling that which is hot have sanitary as well as economic advantages because they do not expose milk on the large coolers where employees may infect it after pasteurization.

Pasteurization in the sealed bottle is not free from disadvantages. The cost of the metal cap varies from three-eighths to one-half cent per bottle. The time required to heat milk in a quart bottle to the required temperature is also important. It is evident that no part of the milk in a bottle ought to be heated above that of the temperature at which pasteurization is stated to take place. For this reason if milk is to be pasteurized at 145 F. the temperature of the water used for heating should not be above 145.5 to 146 F. Furthermore, bottles of milk cannot at once be exposed to the pasteurizing temperature. Carter<sup>2</sup> has reported that for pasteurization in the bottle an air cushion of some 2 per cent. is necessary and when the water in which the bottles of milk is to be pasteurized is held at 152 F. fifteen to twenty minutes are necessary to heat the milk to 150 F.

To further show the length of time required to heat milk in bottles when completely immersed in heated water constantly kept in motion, the accompanying Table 1 of a number of observations is given.

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2. Carter: Pasteurization of milk in the sealed and final package. *Jour. Am. Pub. Health Assn.*, September, 1911.

TABLE 1.—LENGTH OF TIME REQUIRED TO HEAT MILK IN BOTTLES IMMERSSED IN HOT WATER\*

Min.	Pasteurized at 145 F.		Pasteurized at 147 F.		Pasteurized at 149 F.	
	T. of Water	T. of Milk	T. of Water	T. of Milk	T. of Water	T. of Milk
0	116	54	108	53	122	55
5	123	89	116	75	130	85
10	127	105	120	94	141	114
15	132	115	125	105	149	130
20	136	124	131	113	150	139
25	141	130	136	121	149	144
30	145	136	141	128.5	149	146
35	145	140	147	138	149	148
40	145	142	147	142	149+	148+
45	146	144	147	144	149+	149
50	146	145	148	145	...	...
55	...	...	148	146+	...	...
60	...	...	148	147	...	...

\*The observations recorded here are representative of numerous experiments and show that milk in quart bottles does not reach the temperature of the water in which it is immersed for twenty-five to thirty-five minutes.

It is evident that with a spray of water at 146 F. at least thirty minutes must be allowed for warming milk up to 145 F. and pasteurization can only be calculated from that time on. For this reason from sixty to eighty minutes are required for pasteurization in sealed bottles, and after this a cold spray for twenty to thirty minutes is necessary.

Much has been written on the advantages and disadvantages of pasteurization and in the literature are found many studies on this subject. While the primary object of the pasteurization of market milk should be to destroy pathogenic bacteria, determination of the accomplishment of this object is a relatively difficult and slow process. For this reason other more easily determined facts have been taken as evidences of efficient pasteurization. Of these the reduction in bacteria is generally given the foremost rank so that the relation between the number of bacteria present in raw milk and the number killed by pasteurization gives the so-called "efficiency of pasteurization." The rules regulating the pasteurization of milk and milk products for the city of Chicago require that pasteurization must kill 99 per cent. of the bacteria, and all pathogenic bacteria, present. Many of the determinations of efficiency of pasteurization are faulty because plates for counting are made too soon after pasteurization. In a study of a series of experiments on this point the results shown in Table 2 were obtained.

Based on a large series of observations there is no increase in bacteria during the first days of storage at a temperature just above freezing (1 to 2 C.), so that during storage for twenty-four hours the bacteria have not increased; but the low bacterial counts obtained soon after pasteurization are not the true counts for pasteurized milks.

TABLE 2.—DETERMINATIONS OF THE EFFICIENCY OF PASTEURIZATION

Bacteria per c.c. Raw	Method	Pasteurized	
		Bacteria per c.c. Immediately after Pasteuriz.	Bacteria per c.c. After 24 Hrs. at 1 C.
.....	.....		
.....	.....		
31,000	Sealed Bottle, 145 F. 20 min.	300	1,200
280,000	Bulk, 145 F. 20 min.	2,500	15,600
34,000	Sealed Bottle, 147 F. 20 min.	200	840
34,000	Sealed Bottle, 147 F. 30 min.	400	670
48,000	Sealed Bottle, 149 F. 20 min.	0	480
48,000	Sealed Bottle, 149 F. 30 min.	0	670
39,000	Sealed Bottle, 150 F. 30 min.	0	320

It is generally claimed that pasteurization kills the lactic acid organisms and leaves the spores of peptonizing and putrifying bacteria. Many of these statements are not based on personal observation made on pasteurized market milk in this country and have been merely handed down from observations, made especially in Germany where the cream line is not so important, so that pasteurization is carried on at a higher temperature than in the United States. The work of Ayers and Johnson on pasteurized market milk shows that acid-producing organisms are present in this class of milk. During the past year there were received at my laboratory daily deliveries of seven different supplies of certified milk, two of inspected, three of pasteurized market milk, and, for a part of the time, of milk pasteurized at 150 F. for thirty minutes in sealed bottles. The average acidity<sup>3</sup> of all certified milks as delivered was 6.18, of inspected milk 6.306 and of pasteurized milk 5.96 degrees. The average time after delivery at which coagulation appeared when these milks were stored at different temperatures is shown in Table 3.

TABLE 3.—AVERAGE COAGULATION TIME OF MILKS STORED AT DIFFERENT TEMPERATURES

Stored at Temperature C	Coagulation Time after Delivery		
	Certified	Inspected	Pasteurized Market
37 .....	44.2 hrs.	36.8 hrs.	28.7 hrs.
Room .....	4.28 days	3.07 days	3.14 days
Ice-box .....	11.82 days	7.86 days	6.93 days
1 .....	34.07 days	32.1 days	28.5 days

From this table it is evident that at the various temperatures recorded (37 C., room, ice-box and 1 C.), coagulation occurs in pasteurized milk as soon as, or sooner after delivery than in good raw milk. The time here indicated need not represent the age of milk for the pasteurized milks were probably twenty-four hours older than the raw milk at the time of delivery. Generally, too, the acidity of pasteurized market milk is higher, when coagulation occurs, than for good raw milk. Alkaline

3. Degree of acidity equals the number of c.c. of N/4NaOH to neutralize 100 c.c. of milk, using phenolphthalein as the indicator.



reaction was only observed a few times, and then in certified milks stored for some time at low temperatures. Peptonization occurred more frequently in inspected and certified milks than in pasteurized market milk, the change being the most marked when milk was stored at a low temperature.

Besides producing bacteriologic changes, pasteurization may also affect ferments. These are destroyed or rendered inactive at different temperatures so that tests for them are regarded as of considerable importance for the detection of pasteurization and the efficiency of the process. In Germany, where milk is pasteurized at a higher temperature than in the United States, tests for nearly all of these ferments are negative in pasteurized milk. In the United States, however, milk is pasteurized at 140 to 145 F. for twenty to forty-five minutes, so that the so-called "hastened" reductase test of Schardinger and König's catalase tests<sup>1</sup> are practically the only ones that give any evidences of pasteurization of milk as it is delivered to the consumer. For practically all of the other tests milk must be heated to from 70 to 75 C. for twenty minutes. Even the "hastened" or formaldehyd reductase and the catalase tests may be deceptive. Gravity cream always contains the ferments demonstrated by these tests in greater amount than does whole milk, and raw skimmed milk may give negative tests entirely. Moreover, milk from a single cow may not give the "hastened" reductase test. One of the large certified dairies supplying Boston contained a relatively large number of cows whose milk did not reduce methylene-blue in the presence of formaldehyd. Mixed raw milks, however, usually reduced methylene-blue, but a large part of the daily deliveries of pasteurized milk did not reduce methylene-blue and usually the catalase number was small. Apparently some of

#### 1. Reductase Tests:

*Schmidt-Müller or Slow Reductase Test.*—The reagent is made by adding 195 c.c. of distilled water to 5 c.c. of a saturated alcoholic solution of methylene blue (zinc chlorid double salt). This reagent should be boiled every day before using. The test is made by adding to 20 c.c. of milk 1 c.c. of the methylene blue solution, mixing well, then sealing with melted paraffin and holding at 45 to 47 C. in a water-bath. Good milk will not decolorize for twenty-four hours, while milk of high bacterial content will decolorize very quickly.

*Schardinger or Hastened Reductase Test.*—The reagent is made by adding 190 c.c. of distilled water and 5 c.c. of formaldehyde solution to 5 c.c. of saturated alcoholic solution of methylene blue (zinc chlorid double salt). The test is made by adding to 10 c.c. of milk 2 c.c. of the reagent, mixing well, sealing with melted paraffin and holding at 37 C. in a water-bath. Good mixed milk decolorizes after eight to fifteen minutes. Milk from certain cows does not decolorize, nor does milk which has been recently pasteurized at 140 F. or above.

*König's Catalase Test.*—In this test  $H_2O_2$  is added to milk and the oxygen liberated is collected in a graduated tube. In the tests here described, Lobeck's tube was used, the catalase numbers recorded being those obtained when 15 c.c. of milk and 5 c.c. of  $H_2O_2$  were mixed in the apparatus and held at 37 C. for two hours.

the pasteurized market milks at times were under-heated while others were over-heated. Table 4 shows the differences observed in gravity cream, whole milk and skimmed milk.

TABLE 4.—EFFECTS OF PASTEURIZATION ON FERMENTS, AS COMPARED WITH RAW MILK

Specimen	Raw			Pasteurized								
	No. 1	No. 11	No. 12	No. 2	No. 13	No. 4'						
	Hastened Minutes Reductase	Catalase	Hastened Reductase Minutes	Catalase	Hastened Reductase Minutes	Catalase	Hastened Reductase Minutes	Catalase	Hastened Reductase Minutes	Catalase		
Skimmed . . . . .	90	3.0	20	1.4	19	1.6	31	0.2	*	0.4	*	0.0
Mixed . . . . .	5	6.0	9	1.8	10	3.8	9	1.6	25	2.5	*	0.8
Cream . . . . .	1	30.0	—1	9.2	3	18.0	3	5.6	4	4.9	3	6.0

\*None.

Those who have followed the results obtained by a system and method of pasteurization of milk for the market have observed that the results are far from consistent; they are better on one day than on another. This difference is undoubtedly due to the differences in the milks pasteurized. Usually producers of certified milk and inspected milk furnish a product containing fewer bacteria than the maximum allowed, but it does not follow that because milk contains consistently less than 10,000 or 100,000 bacteria per cubic centimeter, the flora is the same from day to day. The differences in the same raw milks of good quality as determined by many examinations are shown in Table 5.

If normal milk of good quality shows such marked variations, how much greater must the variations be in ordinary market milk. That pasteurization cannot wipe out these differences is shown in Table 6, compiled from repeated examinations of three supplies, Numbers 2, 3 and 13, furnishing daily deliveries of market milk pasteurized in bulk by a holding device at 145 F. for twenty or thirty minutes, and one supply, Number 4', of daily deliveries of milk pasteurized in the sealed bottle.

It is quite generally claimed by large milk dealers that the demand for fresh milk is decreasing. This is probably due partly to the increase in the price of milk and the distrust of the consumer resulting from agitation for a better milk-supply. However, coincident with the decreased demand for fresh milk, pasteurization has become more general, but whether pasteurization has had any effect on consumption of fresh milk is not established. The process has not escaped unfavorable criticism. It is certain that much of this criticism can be overcome by official supervision over the milk pasteurized and the process of pasteurization, by pasteurization in the sealed bottle and honest labeling. It

TABLE 5.—SHOWING VARIATIONS IN CERTIFIED AND INSPECTED MILKS AS DELIVERED, RESPECTING BACTERIA, FERMENTS, ETC.

Specimen	Bacteria per c.c.			Per cent. Lactose Fermenters			Per cent. Peptonizers			Glucose* Per cent. Gas	H <sub>2</sub> S Per cent. +	Indol Per cent. +	Gelatin Per cent. Liq.	Catalase			Hastened Reductase (Minutes)			Schmidt-Müller Reductase (Hours)			Degrees of Acidity		
	Average	Highest	Lowest	Average	Highest	Lowest	Average	Highest	Lowest					Average	Highest	Lowest	Average	Fastest	Slowest	Average	Fastest	Slowest	Average	Highest	Lowest
1 ...	3,756	10,500	800	26	70	0	40.8	60	15	40	40	21	90	2.53	3.4	1.4	9.1	5	17	..	1:00	60%	6.00	7.0	4.8
7 ...	6,650	27,000	1,800	33.7	66	8	31.2	50	12	60	50	42	79	2.52	4.2	0.8	8.3	7	19	..	..	100%	5.98	7.0	5.2
8 ...	8,935	24,000	1,400	58.0	80	30	16.0	20	8	50	63	42	84	2.26	2.4	1.2	...	..	..	..	1:30	43%	5.95	7.0	4.4
9 ...	20,650	51,000	3,500	37.2	70	5	11.5	30	0	30	40	44	90	2.0	2.6	1.2	...	..	..	..	..	100%	6.26	7.4	5.6
10 ...	13,900	52,000	900	31.4	50	14	15.8	40	0	10	60	33	89	1.92	2.8	1.4	...	..	..	..	..	100%	6.38	7.6	5.2
11 ...	3,543	14,000	600	39.0	85	10	38.1	90	16	0	63	0	58	1.63	2.0	1.2	10.7	7	22	..	..	100%	6.37	8.0	5.2
14 ...	3,470	7,100	800	33.2	70	10	43.2	80	7	100	70	50	58	1.8	2.2	1.0	9.4	17	4	..	5:00	80%	6.6	7.2	6.0
Ave. .	7,246	52,000	600	35.6	80	0	29.6	90	0	41.43	54.5	30.3	78	2.1	4.2	0.8	...	5	—	..	1:00	—	6.18	8.0	4.4
4 ...	33,610	52,000	12,500	20.1	48	0	16.3	28	1	50	50	100	90	3.06	4.0	2.4	10.1	8	13	..	2:00	40%	6.23	8.0	5.2
12 ...	11,545	99,000	1,300	45	80	40	18.0	50	5	60	80	88	88	2.78	4.8	1.2	13.1	8	44	..	2:30	80%	6.41	6.8	6.0
Ave. .	21,731	99,000	1,300	32.5	80	0	16.9	50	1	55	65	94	88	2.92	4.8	1.2	11.5	8	44	..	2:00	—	6.306	8.0	5.2

\*Glucose fermentation tubes and gelatin inoculated with 1 c.c. of milk and 0.1 c.c. of milk used to inoculate sugar-free broth for determination of hydrogen sulphid and indol production.

Numbers 4 and 12 are inspected milks; the others are certified milks.

†The figures in this column show the longest time taken to decolorize the specimen. The percentage figures show what per cent. of specimens were negative or failed to decolorize. This applies also to Table 6.

TABLE 6.—TESTS SHOWING VARIATIONS IN PASTEURIZED MARKET MILK

Specimen	Bacteria per c.c. —			Per cent. of Lactose Fermenters			Per cent. of Peptonizers			Glucose Produced Per cent.	H <sub>2</sub> S per cent. +	Indol per cent. +	Per cent. Liq.	— Catalase —			Hastened Reductase (Minutes)			Schmidt-Müller Reductase (Hours)			Degrees of Acidity		
	Average	Highest	Lowest	Average	Highest	Lowest	Average	Highest	Lowest					Average	Highest	Lowest	Average	Fastest	Slowest	Average	Fastest	Slowest	Average	Highest	Lowest
2 ...	310,250	840,000	6,000	34.1	80	0	13.7	60	0	100	89	100	100	1.23	1.6	0.2	..	9	60%	..	4:30	50%	5.69	8.0	4.0
3 ...	285,875	1,640,000	16,000	29.3	70	8	42.3	50	20	100	50	89	79	1.7	2.5	0.8	..	110	80%	..	3:00	30%	5.97	7.6	5.2
13 ...	916,333	1,560,000	4,000	38.3	50	20	38.0	80	15	60	70	100	79	1.7	2.5	0.6	..	25	40%	..	12:00	60%	6.36	8.2	6.2
Av. 2,3,13	480,712	1,640,000	4,000	33.2	80	0	32.0	80	0	84	73.3	93	90	1.64	2.5	0.2	..	9	—	..	3:00	—	5.99	8.2	4.0
4' .....	4,020	9,700	200	29.6	70	0	18.6	50	0	10	30	0	100	0.98	1.4	0.6	..	20	80%	..	....	100%	6.08	6.2	6.0

cannot be hoped that pasteurized dirty milk can be made as good as pasteurized clean milk, nor can a uniform product be expected by pasteurization of market milk. The temperature and time for which any particular milk is pasteurized must be sufficient to kill the pathogenic microorganisms of diseases transmissible through milk, must destroy or inactivate the ferments as little as possible, make the process successful economically and preserve the cream line. Most authorities state that 140 F. for twenty minutes will kill all organisms of infectious diseases transmissible by milk. Pasteurization at this temperature and time are undoubtedly correct in the laboratory, but as soon as pasteurization is not carried on in the laboratory it is no longer accurate or scientific. In dairies pasteurization must be left to employees who have only pride and sense of responsibility to the employer as incentives to make them careful. The conditions in pasteurization in bulk are far from those observed in the laboratory where 140 F. for twenty minutes is found to be efficient. In sealed bottles the technic can be made to resemble laboratory technic but even pasteurization in sealed bottles alone is not sufficient; for pressure for time may lead to overheating or underheating and shortening of the length of time of pasteurization. This can only be overcome by timed and regulated devices, the control over which should be left to responsible governmental officials. At least thirty minutes should be allowed for heating, and pasteurization after that should be carried on for thirty minutes more. In dairies the temperature of pasteurization should be at least 145 F. so as to be certain that 140 F. is always reached. The inactivating of some ferments occurs at 140 F., but from a number of observations it seems that they are not as readily inactivated in sealed bottles. While the number of observations made in my laboratory is still too small to venture a definite opinion, a table showing some of the results is given here (Table 7).

From Table 7 it is also seen that heating to 145 F. for thirty minutes affects the ferments but little.

In order to make the process successful economically milk pasteurized in sealed bottles under official supervision should be regarded as a *preferred milk* and bring a higher price than the same milk in the raw condition. At present pasteurization is largely used by the dealer and regarded by the consumer as a process for preservation and making some milks salable. Modifications of machines used by brewers are now quite economically used in some dairies. In the United States most of our people do not buy a particular milk because it is clean or because of the fat it contains, but because of the cream that rises in the bottle. In the sealed bottle pasteurization at 145 F. for thirty minutes does not prevent the formation of the cream line, while heating to 147 F. for twenty to thirty minutes makes it somewhat less distinct and 149 F. for twenty minutes destroys it almost entirely.

TABLE 7.—RESULTS OF TESTS OF RAW MILK AND MILK PASTEURIZED IN SEALED BOTTLES AT VARIOUS TEMPERATURES AND PERIODS

Hastened Reductase Minutes	Storch*	W. & P.	Guaiac	Bellei's Test*		Hastened Reductase Minutes	Storch*	W. & P.	Guaiac	Bellei's Test*
Raw						147 F. 30 Min.				
Skim .. 27	....	....	....	....	Skim .. 59	....	....	....	....	....
Mixed .. 18	Blue	Blue	Blue	Red	Mixed .. 47	Gray	Gray	Neg.	Pink	....
Cream .. 7	....	....	....	....	Cream .. 21	....	....	....	....	....
145 F. 20 Min.					149 F. 20 Min.					....
Skim .. 35	....	....	....	....	Skim .. 51	....	....	....	....	....
Mixed .. 25	Blue	Blue	Blue	Red	Mixed .. 37	Gray	Neg.	Neg.	Slight Red	....
Cream .. 15	....	....	....	....	Cream .. 22	....	....	....	....	....
145 F. 30 Min.					149 F. 30 Min.					....
Skim .. 39	....	....	....	....	Skim .. 63	....	....	....	....	....
Mixed .. 30	Blue	Gray	Blue	Red	Mixed .. 50	Gray	Neg.	Neg.	Slight Red	....
Cream .. 17	....	....	....	....	Cream .. 20	....	....	....	....	....
147 F. 20 Min.					150 F. 30 Min.					....
Skim .. 32	....	....	....	....	Skim .. 50	....	....	....	....	....
Mixed .. 26	Blue	Gray	Blue	Red	Mixed .. 47	Gray	Neg.	Neg.	Slight Red	....
Cream .. 15	....	....	....	....	Cream .. 21	....	....	....	....	....

*\*Storch Test.*—The test is made by adding to 5 c.c. of milk one drop of 0.2 per cent.  $H_2O_2$  and two drops of a 2 per cent. solution of paraphenyldiamin and thoroughly mixing. The reagent must be freshly made at least every two weeks.

*Wilkinson and Peters Test.*—This test is made by adding to 10 c.c. of milk 2 c.c. of a 4 per cent. alcoholic benzidin solution and two or three drops of acetic acid, then mixing well and adding 2 c.c. of 3 per cent  $H_2O_2$ .

*Guaiac Test.*—The reagent is made by adding one part of guaiac to ten parts of acetone. To make the test several drops of 0.2 per cent.  $H_2O_2$  and 1 c.c. of the guaiac solution are added to 10 c.c. of milk. The reaction appears in one to three minutes.

*Bellei Test.*—The test is made by adding to 10 c.c. of milk 3 drops of 1.5 per cent. aqueous solution of ortol and 2 drops of 3 per cent  $H_2O_2$ .

#### CONCLUSIONS

Based on observations and study of various pasteurizing devices and results obtained by them it is evident that the results derived in the laboratory cannot be transferred directly to the dairy.

A routine of 140 F. for twenty minutes while efficient in the laboratory is not a safe one in the dairy.

The safest method for pasteurizing is in the sealed bottle, allowing at least thirty minutes for heating to the temperature of pasteurization and then pasteurizing at 145 F. for thirty minutes — all done under official supervision.

Laboratory men not acquainted with commercial conditions should refrain from advising on the new departure of pasteurizing in the bottle, so that milk producers and dealers will not needlessly have to expend as much money for these devices and systems as a result of what they regard as expert advice as they have for pasteurization devices in the past.

## JUVENILE TABES \*

GEORGE E. PRICE, M.D., AND C. E. G. SHANNON, M.D.

PHILADELPHIA

Juvenile tabes is a rare disorder, being so infrequent that one need not apologize for the report of a single case. In the neurologic dispensary of the Jefferson Hospital there has been one patient with this disease in the past six years, and but one case of juvenile paresis. The latter affection is more common than juvenile tabes, which it not infrequently complicates.

### CASE REPORT

The following case was referred to one of us (Dr. Shannon) by the Children's Bureau on the eleventh day of April, 1911:

*History.*—M. S., a school girl of 14, presented evidence of almost total blindness in both eyes, up to her eleventh year. With the exception of the usual diseases of childhood, she enjoyed perfectly good health. In that year she suffered from an attack of tonsillitis lasting two weeks. Ten days later she was attacked with diphtheria but made a complete recovery in a few weeks.

At the end of six months she began to notice a dimness of vision for all near work. She was at once sent by the school physician to the City Hall and there glassed under drops. These glasses apparently relieved completely the failing vision and at the end of two months she discarded them, believing her sight fully restored.

For over a year her eyes gave her no trouble whatever. At the end of this period, however, she complained of seeing "various colors before her eyes," a condition seriously affecting her sight, which has gradually become worse and persists up to the time of this report.

She visited the Wills Eye Hospital a few weeks following the development of this symptom and the surgeon in attendance informed her of the acutely serious condition of her eyes and gave a very unfavorable prognosis. At that time her vision had been reduced to such an extent that large letters only could be read.

No internal treatment was advised, so she says. Later she consulted the eye department of the Episcopal Hospital and was given internal medication, which she followed for one week only. A short time afterwards she fell into the hands of the Children's Bureau.

The family history on the father's side is negative. On the mother's side, however, we found some suggestive features. Married at the early age of 17, her mother is said to have drunk heavily prior and subsequent to her marriage. On several occasions she had been placed in the House of Good Shepherd and her record reveals a history of a very dissolute life covering many years. She is still living and as far as could be ascertained from the records at the Bureau, despite her past irregular mode of living, enjoys good health. No history of specific disease was obtained, but she had one miscarriage. The patient has one brother and two sisters, all of whom are living and in excellent health.

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\*Read before the Section on Ophthalmology, College of Physicians of Philadelphia, Jan. 18, 1912.

*Examination.*—The patient is well nourished and her musculature normal. She has had since the onset slight occasional headaches and for the past few months considerable headache which, however, has not interfered with her sleep. At times she has complained of sharp, stabbing pains in her knees, and for the past one and one-half years has had more or less urinary incontinence.

Her eye condition is as follows:

*Lids.*—No disease referable to the lid was observed.

*Muscle.*—Divergence of O. S. outward and upward. Difficult rotation to left, attended with slight rotatory nystagmus. No history of diplopia.

*Vision.*—Reduced in each eye barely to light perception.

*Pupils.*—Unequal; O. D. 3.5 mm., O. S. 3 mm. With atropin 7.5 mm. in each eye. They did not respond to direct nor indirect stimulation. Argyll-Robertson pupil could not be demonstrated. The eyes were quite sensitive to light.

*Ophthalmoscopic Examination.*—This showed a complete primary optic atrophy of each disk. The margins of the papillæ were very distinct. In other respects the appearance of the fundus was negative. The patient was then referred to Dr. Price for neurologic examination.

*Neurologic Examination.*—The gait and station were normal. There was no weakness of the facial muscles nor involvement of any of the cranial nerves other than the optic. Grip with both hands was strong but there was slight ataxia of the upper extremities. Weakness of the bladder sphincter was present. The patella tendon and Achilles tendon reflexes were absent. There was no ankle clonus nor Babinski sign and no hysterical stigmata. Sensation was unimpaired and there was no muscular atrophy. A diagnosis of juvenile tabes was suggested and a Wassermann test was advised. This was subsequently made by Dr. E. Burville Holmes who reported a positive reaction.

A report on the cerebrospinal fluid by Dr. George F. Lull, June 19, 1911, was as follows: Reaction alkaline; specific gravity unobtained on account of an insufficient quantity of the fluid. Albumin was increased; urea was absent. Microscopic examination revealed the presence of a few endothelial cells, the lymphocytes, however, were not increased. No bacteria were found.

Remak,<sup>1</sup> in 1885, was the first to call special attention to the disorder, many cases having since this time been reported in all parts of the globe.

The subject of locomotor ataxia in the young presents many interesting features, among which may be mentioned the relative infrequency of marked ataxia, the unusual prevalence of optic atrophy and the fact that females are affected more often than males. Although cases have been reported as resulting from acquired lues, transmitted syphilis is the overwhelming etiologic factor of juvenile tabes.

The average age at which the disease appears is about 15 years, although Marburg<sup>2</sup> has reported a case in an infant of 2 years, and cases of tabes from hereditary syphilis have been reported that did not develop until adult life. Cantonnet<sup>3</sup> comments on the "striking and as yet unexplained contrast to the sex incidence in later life," and gives the following figures as to the relative frequency of the disorder: females 62.6 per cent., males 37.3 per cent. Gower has given the ratio for adult tabes as ten

1. Remak: Berl. klin. Wehnschr., 1885, No. 7.

2. Marburg: Wien. med. Wehnschr., March 21, 1908.

3. Cantonnet: Arch. d'opht., November, 1907.

males to one female, but as this proportion is about the same as that of male to female syphilitics, we find that of those exposed to lues, the proportion developing tabes would be about equally divided between the sexes. In juvenile tabes, hereditary syphilis being the etiologic factor, the sexes would be equally liable. This we believe would explain the contrast in part, but not entirely.

According to Ernest Jones,<sup>4</sup> no symptom occurs in adult tabes that has not been observed in juvenile tabes. Urinary incontinence is present in nearly 60 per cent. of cases and is frequently the earliest symptom of the disease. It is a striking fact that marked ataxia is a comparatively rare symptom and "Benedikt's axiom," that ataxic symptoms disappear or fail to develop after the appearance of optic atrophy, is distinctly applicable, as optic atrophy is present in so large a proportion of the cases.

Disturbances of the eye are so frequently associated with the development of tabes that a careful ocular examination is of the greatest importance in this condition. The extreme rarity of this disease may be appreciated from the fact that Otto Marburg in 1903 collected but thirty-four cases from all the literature on the subject. Cantonnet's<sup>5</sup> analysis of eighty-nine cases of juvenile tabes is perhaps the most exhaustive so far presented and his conclusions are of extreme interest. He tabulates the following eye symptoms: (1) inequality of pupils; (2) Argyll-Robertson pupil; (3) optic atrophy; (4) external ophthalmoplegia; (5) latent ocular ataxy. Cantonnet deduces from his studies of this disease that the prognosis as regards sight is unfavorable, as optic atrophy is so frequent. He finds that juvenile as well as adult tabes takes on numerous clinical manifestations and observes that in the group characterized mainly by amblyopia due to optic atrophy, changes in the pupillary reflexes and abatement of the knee and ankle jerks, that optic atrophy in 14 per cent. was the first sign noted, and in 43.9 per cent. optic atrophy complete or incomplete was present.

Dercum states in this connection that optic atrophy is usually associated with Argyll-Robertson pupil but that it has been noted without the latter, and, indeed, may be the sole evidence of the existence of tabes. Stephenson<sup>6</sup> in his contribution to the *Lancet*, in which he reports four cases of juvenile tabes, avers that in a large proportion of children suffering from amblyopia and optic atrophy, the diagnosis of juvenile tabes could be made with reasonable assurance. Collins thinks that optic atrophy may be seen five years following the beginning of the disease and believes that it starts in the periphery of the retina.

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4. Jones, Ernest: *Brit. Jour. of Child. Dis.*, April, 1908.

5. Stephenson: *Lancet*, London, May 16, 1908.



Mott<sup>6</sup> considers contraction of the visual field and optic atrophy early signs of tabes. A point of controversy prevails as to whether or not the ataxic symptoms of tabes are affected by the early or late appearance of optic atrophy. Gower believes that with optic atrophy occurring early in the disease, as often happens, the late symptoms of tabes fail in many cases to develop. Cantonnet in his investigations finds that in those cases associated with optic atrophy ataxy is not usually seen, as with the appearance of optic atrophy this symptom either disappears or fails to develop. His figures on this point show that among forty cases of optic atrophy, 70.5 per cent. were without ataxy; 20 per cent. with slight ataxy; and 9.5 per cent. with pronounced ataxy. Other observers claim further that the ataxic symptoms even when they have reached a pronounced stage tend to be ameliorated or arrested altogether by the advent of optic atrophy, and cite cases substantiating these conclusions. According to the observations of Andre Leri (Posey and Spiller) and Collins, however, tabes is uninfluenced by the onset of optic atrophy early or late in the course of the disease. That stage of tabes in which optic atrophy makes its early appearance is frequently called by oculists the pre-ataxic stage and the importance of a correct diagnosis cannot be overestimated so that the patient may receive suitable treatment at once. Hereditary optic atrophy generally affecting the younger members of a family at the age of puberty need cause no confusion in the way of diagnosis, as the visual field is unaffected save by the appearance of central scotomata.

The eye symptoms in juvenile tabes correspond in a great measure to those observed in the adult type. Muscle palsies are common. They are usually isolated, develop suddenly and disappear from within a few hours to two or three weeks. Occurring in the early course of the disease, this is the usual case according to Posey,<sup>7</sup> but in the later stage they tend to be permanent, although they may be transient like those of the earlier stage. The muscles governing the associated movements are rarely if ever involved. Varying opinions prevail as to the muscles most frequently affected, although most observers agree on the external rectus, the levator palpebrarum, the muscles governed by the third nerve, as among the first to be affected by the palsy. As regards the involvement of the coats of the eye in juvenile tabes, Cantonnet states that of those cases in which there was evidence of inherited and acquired syphilis 13.9 per cent. presented personal stigmata in the form of retinochorioiditis and interstitial keratitis. It is interesting to note in this connection that Syndacker<sup>8</sup> states that in nearly 100 per cent. of tabetics examined carefully, no evidence of iritis or chorioiditis could be found. In fact, Wernicke

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6. Mott: *System of Syphilis*, iv.

7. Posey: *Jour. Am. Med. Assn.*, Chicago, 1910, liv, 1277.

8. Syndacker: *Jour. Am. Med. Assn.*, Chicago, 1910, liv, 933.

goes so far as to say that "syphilitics who have suffered from specific iritis or chorioiditis do not acquire tabes."

Lightning pains appear about as frequently as in the adult form, while visceral crises are present in from 17 to 20 per cent. of cases. Marburg has reported a case of juvenile tabes with laryngeal crises. The girdle sensation is not frequently observed and trophic symptoms, such as the Charcot joint and perforating ulcer of the foot, are rare. A case of juvenile tabes with a Charcot joint was reported by Nonne.<sup>9</sup> Malling<sup>10</sup> reports four cases of juvenile tabes with autopsy.

Lymphocytosis and excess of albumin in the cerebrospinal fluid have been found in one case by Hirtz and Lemaire.<sup>11</sup>

The course of this affection, like that of adult tabes, is chronic and the prognosis, therefore, is good as to life. The frequency with which optic atrophy and blindness occur, however, should cause one to be very guarded in the prognosis as to vision.

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9. Nonne: *Syphilis und Nervensystem*, Berlin, 1902, p. 404.

10. Malling, K.: *Monatsh. f. Psychiat. u. Neurol. Berl.*, 1910, xxviii, 304.

11. Hirtz and Lemaire: *Bull. et mém. Soc. méd. d. hôp. de Paris*, Oct. 27, 1904, p. 974.

## ACUTE GLANDULAR FEVER IN CHILDREN \*

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Despite the fact that more than a score of years have passed since E. Pfeiffer<sup>1</sup> first read a paper describing the condition which he termed (Drüsenfieber) glandular fever, to which Filatow<sup>2</sup> had called attention four years earlier, and although the picture has since been seen and recognized by numerous observers, and many papers written on the subject, there is still discussion as to whether such condition exists as a disease sui generis; or whether it but represents a state of glandular enlargement, secondary to infection of the nasopharynx and mouth; or perhaps an atypical or abortive form of some disease having glandular swelling as an accompanying symptom.

The observation of an epidemic and a review of the literature must convince one that a disease such as Pfeiffer described does exist, at least as a clinical entity; the etiology, however, is still obscure.

The chief argument of those opposed to the idea that the condition is a separate disease, among whom are Hochsinger,<sup>3</sup> Zappert,<sup>4</sup> and Trautmann,<sup>5</sup> is that the glands involved drain the nose, nasopharynx, pharynx and mouth, and through these the more distant groups of glands become affected. Hence the symptom complex is only a manifestation of glandular enlargement due to a regional infection of one or more of the foregoing areas.

Although this may be entirely true, the reaction of the glandular system to such an infection is so distinct and characteristic that there is certainly as much justification for speaking of glandular fever as there is for speaking of scarlet, measles or röteln, which are after all only the skin manifestations of mucous membrane infections, and of the same area as that involved in glandular fever.

The symptoms characterizing the condition and which refuse to fit into any other disease niche are fever and malaise, *acute swelling* and

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\*Read before the Pediatric Section of the N. Y. Acad. Med., Dec. 14, 1911.

1. Pfeiffer, Emil: Drüsenfieber. Jahrb. f. Kinderh., 1890, p. 461.

2. Filatow: Acute Infectious Diseases of Childhood, 1885.

3. Carl Hochsinger: Das sogenannte Drüsenfieber der Kinder. Wien. med. Wehnschr., 1902, p. 258.

4. Zappert, J.: Ueber einige dem Kindesalter eigenthümliche Erkrankungen der Nase, etc. Deutsche Klin., 1905, vii, 590.

5. Trautmann, G.: Beitrag zum Wesen des Drüsenfiebers, unter Berücksichtigung der Bakteriologie, Jahrb. f. Kinderh., 1904, p. 503.

TABLE 1.—ANALYSIS OF AUTHOR'S CASES OF GLANDULAR FEVER

Case	Sex	Age, Years	Date, 1911	Duration, Days	Children in Family	Invasion, Hours	Symptoms at Onset, Fever, etc.	Bowels	Naso-Pharynx	Pharynx	Abd., Tender	Liver, Palp.	Spleen, Palp.	Torticollis	Cough	Maximum Temperature	Temp. dropped, Day	Recurred	Maximum Pulse	Apex Syst. Murmur.	2nd Day
1 A. R.	F.	3½	4/16	24	2	0	Irritable Anorexia	Constipated	+	+	+	+	+	+	+	104.8	7	3	150		
2 H. R.	F.	2	2/20	35	2	48	Irritable	Normal	+	+	+	+	+	+	+	102	15	Pus	120		
3 H. E.	M.	3¼	2/28	2	..	0	.....	Normal	+	+	+	+	+	+	+	102	2	+	120		
4 C. M.	M.	4	4/16	16	1	48	Irritable Anorexia	Constipated	+	+	+	+	+	+	+	102	6	+	120		
5 W. D.	F.	4½	4/17	10	1	12	Anorexia	Normal	+	+	+	+	+	+	+	102.5	8	+	140		6th.
6 G. H.	M.	4	4/5	19	2	24	Langnor	Constipated	+	+	+	+	+	+	+	101	6	+	110		
7 K. M.	F.	8	4/21	11	2	48	Irritable Anorexia	Constipated	+	+	+	+	+	+	+	103.5	16	*	140		
8 K. B.	M.	5	4/25	7	..	24	Langnor	Normal	+	+	+	+	+	+	+	101	7	..	110		
9 P. G.	M.	5	4/27	7	1	0	Anorexia	Constipated	+	+	+	+	+	+	+	102.6	6	..	120		4th.
10 H. M.	M.	4¾	4/12	14	1	12	Langnor	Constipated	+	+	+	+	+	+	+	103	6	..	110		
11 R. H.	M.	3¼	4/26	?	1	0	Irritable	Normal	+	+	+	+	+	+	+	103.4	12	Pus	140		1st.
12 F. J.	M.	6	4/18	24	1	48	Vomiting	Constipated	+	+	+	+	+	+	+	103	8	+	120		

\*Follicular tonsillitis followed.

tenderness of the *glands of the neck* accompanied by a lesser involvement of the entire glandular system; a rapid recession of symptoms, with a return of the glands to normal size, or in some instances repeated exacerbations of fever, and enlargement of glands before complete recovery takes place.

The disease occurs in sporadic and epidemic form. The latter seems the more common, probably because the single cases go unrecognized, being classified as adenitis. Park West<sup>6</sup> described the largest epidemic, ninety-six cases among forty-three families, extending over a period of three years from 1893 to 1896. Many other smaller epidemics have been reported. The last with an excellent review of the literature by Kay Schäffer<sup>7</sup> from the Küstenhospital in Refsnäs, Denmark. In four months twenty-one children ranging in age from 4 to 15 years were observed among the inmates of the institution.

In New York City in the spring of 1911 there was an extensive epidemic. In my private practice from February 20 to May 12 there occurred twelve cases in ten families. In the out-patient services of Vanderbilt Clinic and Lebanon Hospital, many other cases were seen, but owing to the lack of adequate data, mention of these will only be made for points of special interest.

TABLE 2.—SHOWING LOCATION AND CHARACTER OF THE GLANDULAR ENLARGEMENT IN THE AUTHOR'S CASES

Case	Superf. Network	Parotid	Angle	Post Cerv.	Sub- Maxill.	Sub- Ment.	Supra Clav.	Axill.	Epitroc.	Inguin.	Tender
1	+	..	++	+	..	..	+	+	..	..	++
2	+	+	++++	+	+	..	..	..	..	..	++
3	+	..	++	+	+	..	..	..	..	..	++
4	..	..	++	+	+	..	++	+	+	+	..
5	+	++†	++	+	..	+	..	+	..	+	+
6	+	+	++	+	..	..	..	+	..	+	+
7	+	..	++	+	..	..	..	+	..	..	++
8	..	..	++	+	..	..	..	..	..	..	+
9	+	..	+	+	+	..	..	..	+	..	..
10	+	..	+	+	..	..	..	..	+	..	..
11	+	..	++	+	..	..	..	+	+	..	+
12	+	..	++++	+	+	+	+	+	+	+	++

+ = Size of bean; ++ = pigeon egg; +++ = hen's egg; ++++ = goose egg.

\*Crosses in second, third and last columns do not refer to size, but to the presence of symptoms.

†Exposed to parotitis two weeks before.

A study of the previous history of these cases developed the interesting fact that symptoms of the exudative diathesis existed in every instance, as shown in Table 3. Perhaps this condition may prove

6. Park West: An Epidemic of Glandular Fever, Arch. Ped. September, 1896, p. 889.

7. Schäffer, Kay: Eine Epidemie von Febris Glandularis. Jahrb. f. Kinderh., 1909, p. 526.

to be a predisposing factor, should further experience substantiate this observation.

TABLE 3.—SHOWING PREVIOUS HISTORY OF AUTHOR'S PATIENTS

Case ....	Ade- noid	Hyp. Tonsils	Ade- nitis	Oti- tis	Acido- sis	Eczema .....	Rheumat- ism	Spasmodic Group
1	+	+	+	+	+	..	..	+
2	+	+	+	..	++	++	..	..
3	+	..	+	+	..	++	..	..
4	+	..	+	+	+	+++	..	..
5	..	..	+	+	+	Urticaria	..	++
6	..	..	+	+	+	....	..	..
7	*+	++	+	..	..	....	+	..
8	*+	+	..	..	..	....	..	..
9	+	..	+	+	+	....	..	..
10	*+	+	+	†+	..	....	..	..
11	..	..	+	..	Convulsions	+	..	..
12	*+	+	+	+	..	+	..	+

\*Operation on account of tonsils and adenoids. †Mastoid operation.

#### CONTAGIOUSNESS

That the condition is contagious would appear from the fact that house epidemics have been reported by Pfeiffer, Rauchfuss<sup>8</sup> and others. Hospital epidemics may occur as described by Schäffer, and when the disease enters a household where there are other children, one or more of them usually becomes affected.

Schäffer states that an epidemic of influenza ran through the hospital concurrently with his cases, beginning after ten cases of glandular fever existed, lasting five weeks. Nine other cases of glandular fever arose during this period, and two after the influenza epidemic which affected twenty-six cases had subsided. Two patients, girls, contracted both diseases, one affected three weeks after, the other four weeks before the glandular fever.

#### ETIOLOGY

It is essentially a disease of early childhood although cases are reported among adults. The overwhelming number occurs under the age of 10, and most of these under the age of 5 years.

I saw in the spring of 1911 two cases in infants of 5 and 10 months, respectively. The photograph is of the one 5 months old.

Sex: There seems to be no predilection for either sex.

The social condition does not seem to be a factor. Most cases occur during the winter and spring months.

#### PATHOLOGY

The pathology is still obscure, although the evidence seems to point to the possibility of a streptococcus infection, at least as the cause of

8. Rauchfuss: Zur Kasuistik des Drüsenfiebers, Jahrb. f. Kinderh., 1890, p. 461.



complications. That more than one organism may be responsible for the condition is not unlikely. An attempt has been made to determine this factor by taking cultures from the nose and throat of patients suffering from the disease, but the result has been unsatisfactory. Streptococci, staphylococci, pneumococci and influenza bacilli have been found, as might be expected. Cultures taken from the pus of cases in which the glands had broken down, gave a more regular result. Schäffer found in the pus of two cases streptococci in pure culture, and saw a third case which developed erysipelas at the site of a tuberculous fistula arising among the affected glands; i. e., a streptococcus infection.

Botschkowsky<sup>9</sup> found streptococci in two cases in pure culture. Neumann<sup>10</sup> found streptococci and staphylococci in one case and in a number of other cases streptococci alone.

Korsakoff<sup>11</sup> in an autopsy of a case of glandular fever found streptococci in pure culture in the cervical and axillary glands, liver, spleen, kidneys, medulla of bones and heart-blood. The glands showed acute parenchymatous hyperplasia with largely dilated blood-vessels. Korsakoff took cultures from the urine of five cases complicated by nephritis; in two he obtained a negative result; in the other three streptococci in pure culture were found.

In one of my cases in which a culture was taken of the pus from the broken-down glands, streptococci were found in pure culture.

Tschaiskowsky<sup>12</sup> found the influenza bacilli in the glandular tissues and the blood, but the growths were planted on ordinary agar and carried through several generations, no blood having been added to the culture medium. For this reason his findings have been questioned.

The incubation period, according to Park West, is about seven days, although this is not at all certain.

The invasion is usually sudden although malaise, slight temperature and perhaps vomiting may precede outbreak by a day or two.

#### INITIAL SYMPTOMS

A child is taken suddenly ill with fairly high temperature, or has had a little fever for a day or two, and then a sudden exacerbation of temperature. A variable degree of prostration, pain in limbs, headache, considerable irritability, a moderately rapid pulse, occasionally vomiting. There is usually pain in the throat and often in the abdomen as well. Physical examination shows a child with face somewhat flushed, irritable

9. Botschkowsky: Cited by Korsakoff, *Arch. f. Kinderh.*, 1905, p. 193, 321.

10. Neumann: *Ueber acute idiopathische Halsdrüsenentzündungen*. Berlin. klin. Wehnscr., 1891, p. 1227.

11. Korsakoff: *Beiträge zur Lehre vom Drüsenfieber*. *Arch. f. Kinderh.*, 1905, p. 193, 321.

12. Tschaiskowsky: Cited by Korsakoff; see Note 11.

and restless. Often a slight coryza. Pharynx slightly congested or normal; temperature 101 to 105 F.; pulse 100 to 140; respiration in normal ratio to the temperature and pulse. At the angle of the jaw, usually on the left side, is found a slightly enlarged gland (almond size) which may be extremely tender to the touch and may, even in this stage, cause the head to be held rigid in position of torticollis, and produce pain on swallowing. The chest and circulatory system at this time are usually negative. The abdomen, however, is often the seat of pain in its lower half. Pfeiffer believed that in the more severe cases "the majority complain of pain in the abdomen which is always exactly in the median line and exactly midway between the umbilicus and the symphysis pubis." This latter statement has since been found to be incorrect, although the pain is usually below the umbilicus; it may be anywhere, or all over this area.



Fig. 1.—Infant aged 5 months, with glandular fever.

The appetite is diminished, bowels usually constipated, rarely diarrhea. A number of observers have reported eruptions on the skin which is, however, not characteristic and very infrequent.

Thus far there is nothing characteristic in the condition; but within twelve to forty-eight hours in the typical cases the single gland at the angle is masked by a large mass, extremely tender, just beneath and posterior to the upper end of the sternomastoid muscle, varying in size from pigeon to goose egg. Glands (pea size) form a chain along the posterior border of the same muscle. The enlargement of these two sets of glands is by most writers on the subject considered more or less pathognomonic without, however, it appears to me, sufficient justification, since they are at times involved in other conditions.



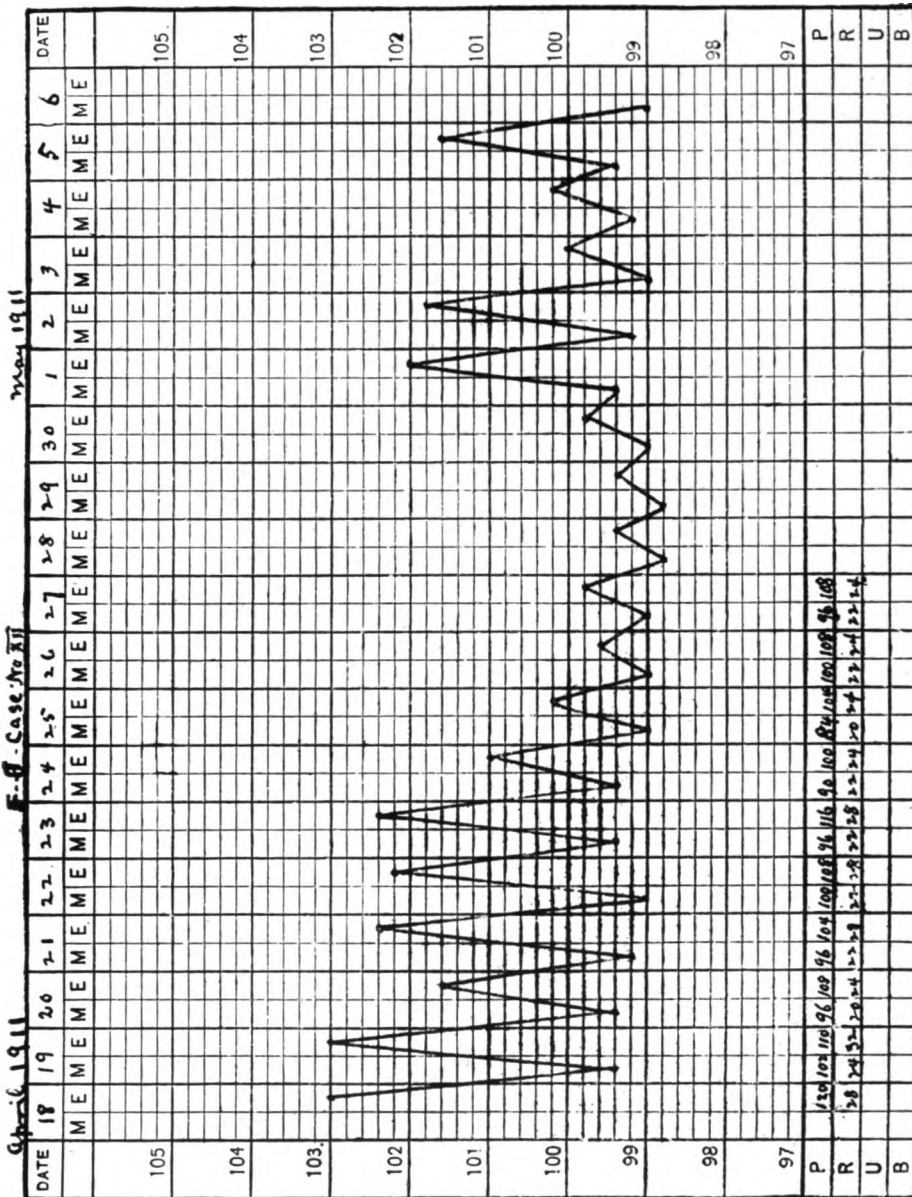


Fig. 2.—Chart showing temperature curve, pulse and respiration in Case 12.

The glands along the anterior border of the sternomastoid muscle, the posterior cervical, the supraclavicular, the submental, submaxillary anterior and the parotid glands are enlarged, and a fine network of glands about 1 cm. in diameter, like the spots placed at the intersection of the strands of a large mesh veil, covers the entire lateral and posterior aspects of the neck.

Besides these, the axillary, epitrochlear, inguinal and mesenteric glands are frequently enlarged and tender. It is surprising how much pain is complained of on grasping these patients in the axillæ where the glands are only just palpable. The mesenteric glands can often be felt enlarged. Park West found them palpable in thirty-seven of his cases. That the retro-esophageal and bronchial glands are also often enlarged hardly admits of doubt, since it is not uncommon to find severe pain and difficulty in swallowing, and a croupy cough in these cases, beginning with the swelling and terminating with subsidence of those glands which are palpable.

The glandular swelling is bilateral, although not always synchronous.

The liver and spleen in a certain number of cases become palpable after a few days, but not regularly, as some observers state. The temperature is very irregular, often rising and falling several times in one day, the rise usually being followed by the enlargement of some gland.

#### COURSE

The course usually follows one of four types:

1. The glands grow suddenly large, with the appearance of fever and prostration. The latter symptoms disappear in the course of one to three days, the glands diminishing in size more slowly as a rule, but often subsiding in a day.

2. After one or more days of moderate fever and malaise, a sudden rise in temperature to 104 to 105 F. occurs with glands which grow large soon after, until they assume the size of goose eggs or smaller, and after four to seven days the attack subsides, the glands receding slowly, sometimes taking several weeks.

3. The onset may be sudden, or after a period of invasion a set of glands becomes enlarged, with rise of temperature which subsides after two or three days to 99 to 100 F., remaining around the normal for a variable time — one to four days — to suddenly jump again to 103 to 105, which rise is soon followed by the swelling of other glands.

It is possible to have the same group swell and subside several times. This state of alternate periods of well-being with normal temperature, and prostration with fever, glandular swelling, and pain may continue for weeks (eight weeks in some cases) and where the glandular enlarge-

ment is slight, the condition may be overlooked and give rise to much anxiety.

4. The glands enlarge and become tender, without any other subjective or constitutional symptoms.

#### PROGNOSIS

The prognosis is good in almost every case, although fatal cases have been reported. The recovery is complete although it may be a long time before all the glands return to the normal size.

Pfeiffer held that none of these cases ever progressed to the point of suppuration; later experience has shown that this is not uncommon.

Two of my own cases in twelve terminated in this way, requiring incision and the evacuation of large quantities of pus, returning promptly to the normal thereafter.

#### DIAGNOSIS

The diagnosis in the typical cases is not difficult. The sudden enlargement of the glands of the neck, with prostration in most cases, with no adequate cause to be found in the nose, nasopharynx or mouth, are characteristic, the glandular enlargement being out of all proportion to any local congestion which may exist.

The sudden disappearance of symptoms with rapid recession in size of the glands involved, the inability to classify the condition otherwise, constitute determining points.

In the less typical cases the diagnosis may offer difficulties, except during an epidemic. In these cases, however, the entire absence of other physical signs, the quick changes in the size and the number of glands involved, the unusual localization under the sternomastoid and along the posterior border and their extreme tenderness, the absence of blood changes characteristic of diseases having unusual glandular enlargement for a symptom, should make the diagnosis.

#### DIFFERENTIAL DIAGNOSIS

This must be made from an adenitis having a distinct local process as its cause either in the nose, nasopharynx, mouth, teeth, scalp, neighboring skin area, or in the underlying tissues; from tuberculous and syphilitic adenitis; from Hodgkin's disease; from leukemia; from parotiditis; from calculi in the salivary ducts; from Mikulicz' disease.

The differential diagnosis between parotitis and this disease is practically impossible, when the parotid glands are involved, as they were in three of my series. The contagious character, course and prognosis are similar, and at least one of my cases, Case 5, had been exposed to parotitis two weeks previous to onset.

Schäffer saw two cases which resembled parotitis; but the swelling occurred several days after the onset, which permitted differentiation. James Cautlie states that the peculiar form of mumps which is supposed to have been "pestis minor" in Astrakan in 1877 was probably glandular fever. Against this conception is the variance in the incubation period, if we can accept West's findings, seven days as against fourteen to twenty-one days in mumps, and that fifty-seven of his ninety-six cases had had or have had mumps since.<sup>13</sup>

Where the glandular enlargement is slight the disease must be differentiated from intestinal disturbances; when the character of the condition is intermittent and prolonged, from pyelitis and malaria; in the presence of painful and difficult swallowing, from a diphtheritic or other infection of the laryngopharyngeal region, and from impacted foreign body; when the abdominal pain and tenderness is marked, from an appendicitis or other intra-abdominal disturbance.

#### COMPLICATIONS

In a small number of the cases a nephritis arises which clears up after the disease has run its course. A systolic mitral murmur arises in many cases after a few days; it is probably hemic in character, as it regularly disappears after recovery. Suppuration of the glands has been recorded above. It rarely occurs in more than one gland mass. Otitis media has been observed.

#### TREATMENT

Unlike most acute diseases confinement to bed is unnecessary except at the onset, and when the temperature is high in the exacerbations. Between these periods the patients may be permitted to be out of bed; isolation, of course, being maintained.

Many cases are so mild as to require no treatment.

The diet may be the usual full diet when appetite is present, as it usually is, except during the periods of high temperature and when the abdominal symptoms are marked.

The temperature requires cool sponging or a tepid full bath; this also reduces the irritability when present.

The local treatment consists of nasal irrigation with saline solution by means of a nasal douche cup, gargling with some mild antiseptic solution and the application of ice bags to the tender, swollen glands, although

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13. Since above was written I have seen a group of five cases in one household wherein one had only the parotids affected, one all but the parotids, and three in which both parotid and other glands were involved. In another household a child had the glands of the neck, the lachrymal, and both submaxillary and parotid salivary glands involved, whereas the mother who contracted the disease had only the parotids and the submaxillary salivary glands affected.

heat in the form of a hot water bag, or hot poultices, is sometimes more effective.

A symptom often complained of when the salivary glands are involved, and not easily relieved, is the dry mouth and peculiarly disagreeable taste, due to the diminished secretion of saliva. Glycerin and lemon juice applied locally, chewing of gum, or the use of sodium iodid gr. 3 to 5 in one-half tumbler of water three to four times daily may be tried.

Hexamethylenamin gr. 5 dissolved in a tumbler of water and taken internally three to four times daily, appears to have some value.

For the persistently swollen glands nothing gives such benefit as arsenic in the form of liquor potassii arsenitis in ascending doses: m. 2 to 10, well diluted with water, three times a day.

Calomel, quinin and other drugs were used without apparent benefit.

The complications when occurring must of course be met according to indications. When the glands break down they are to be incised, after which they rapidly return to normal.

For the anemia which usually follows the disease, fresh air and the use of iron should be ordered.

#### SEQUELÆ

A profound anemia is a regular sequel to the more severe cases; it has been mentioned by nearly all observers, and takes some time to disappear.

Lassitude accompanies the anemia, but disappears before the latter. There are no recorded cases of two attacks occurring in the same individual, although this undoubtedly happens. The following case is of interest as showing the importance of recognizing glandular fever and the necessity of considering it in cases of appendicitis in childhood.

#### REPORT OF CASE 12

*History.*—F. J., a boy, aged 6, with a previous history of measles, varicella, frequent attacks of follicular tonsillitis, and rhinitis; adenoids and tonsils removed February 21, 1911. There had always existed a general slight adenitis.

He was first seen on the evening of April 18, 1911. Two days previously he had vomited, after which he had felt as well as usual until the afternoon of April 18, when he complained of pain in the throat and in the lower part of the abdomen.

*Physical Examination.*—Physical examination showed an irritable child, face highly flushed, temperature 103, pulse 128, respiration 28, tongue clean. The throat was slightly congested; at the angles of the jaw on both sides the glands could be palpated and were the size of small beans. They were excessively tender to the touch, and swallowing was very painful.

There was a croupy cough. The chest was negative; no cardiac murmur. The abdomen was soft, with slight rigidity of the right rectus muscle. The entire abdomen below the umbilicus was tender, more marked, however, in the right iliac region at McBurney's point. Pain was increased when pressure was made here and the extended lower extremity was flexed at the thigh. There was a very distinct "Head zone" extending from the umbilicus to the anterior spine

of the ilium on the right side; none on the left. No mass could be felt; liver and spleen not palpable; bowels moved as usual.

The next day conditions were unchanged except that the tenderness was distinctly at the appendix and the "Head zone" was somewhat less marked. A prominent surgeon was called in consultation; he concurred in the diagnosis of an acute catarrhal appendicitis and advised delay in operating until what was supposed to be an acute inflammation of the upper air passages had subsided. The glands at the angle of the jaw at this time were very little larger than on the previous day. On April 21 the gland at the left angle was the size of a hen's egg; the right somewhat smaller. Along the posterior border of sternomastoid muscle there was a chain of pea-sized glands; anteriorly there was a similar chain. The posterior cervical, submental, supraclavicular, axillary, epitrochlear and inguinal nodes were about the same size and readily palpable. On the posterior and lateral aspects of the neck was the network of small glands referred to elsewhere. All were tender, especially the axillary and inguinal. On April 22, the appendix tenderness and "Head zone" had disappeared. On April 23 all the abdominal tenderness had disappeared. On April 25 the gland at the left angle of the jaw was the size of a pigeon egg, the right only one-half the previous size, and all others smaller, none tender. The cough disappeared shortly after the onset. On April 26 the temperature was normal; glands receding rapidly; patient cheerful and happy.

On May 1 the temperature rose again suddenly to 102 F. The gland at left angle goose-egg, the right pigeon-egg size. Opposite the right lower molars was a gland the size of a marble; others as in first attack; only slight abdominal tenderness.

On the third and fourth the patient was comfortable and happy. On the fifth the same irritable state, abdomen tense, lips swollen, the glands under the angles enormous. This terminated the process; from this time forward the glands receded rapidly, and at the end of two weeks had returned to pea size at the angles; others not felt. A marked pallor and lassitude took two more weeks to disappear.

In Case 5, there were marked abdominal tenderness and pain. The mesenteric glands, owing to the thinness of the abdominal wall, were readily palpable as bodies the size of almonds. These disappeared as the symptoms subsided.

This disease, characterized by fever, prostration, acute, painful swelling of the lymphatic glands, chiefly those of the neck, running a characteristic course, contagious in character, often occurring in epidemic form, the failure to recognize which may lead to false and grave prognosis, is entitled to a place in all text-books on pediatrics which at present fail to mention it, and a fuller consideration in most of those which do.

666 West End Avenue.

## AN ADJUSTABLE METABOLISM BED FOR INFANTS AND YOUNG CHILDREN

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Many forms of apparatus have been devised for the purpose of holding infants and young children in positions suitable for the collection of urine and feces separately. Every investigator who has attempted to place a wriggling, squirming, kicking baby in one position and keep it there for any length of time knows with what difficulty it is accomplished. Many an enthusiastic worker has spent the entire morning trying to corral the subject of investigation only to learn, on turning his back, the truth of Burns' couplet,

The best laid schemes o' mice an' men gang aft a-gley.

Indeed, but recently the originator of one of these holding devices for strenuous young America confessed that after much strapping and adjusting he felt sure that nothing could interfere with the proper collection of material. On his return an hour later imagine his chagrin and surprise to find that the youngster had escaped his leash and was calmly seated in the dish prepared for feces and happily puddling in the urine container.

Many an earnest follower of Voit and Rubner has well-nigh lost his enthusiasm when in the midst of a carefully planned experiment he has received a hasty message that an accident had occurred in the ward and part or all of the material lost. The difficulties lying in the path of one doing metabolism work are many and any devices to lessen them will tend to encourage this most important branch of pediatrics. With this purpose in view I desire to present drawings and photographs of a bed which I have found much reduces the cares attendant on the proper collection of material and at the same time gives to the subject the maximum of comfort.

The drawings are sufficiently clear and comprehensive so that they require no extended description.

Figure 1 shows the various positions to which the frame may be adjusted. Note that the bed may be placed in any position from horizontal to upright; also note the method of changing the length of frame to suit any length of thigh. The full line drawing shows frame adjusted for the smallest infant, while the dotted lines change it for longer thigh. (The end containing the flask is at the foot of the bed.)

Figure 2 represents the piece of heavy canvas to be laced to the frame, the small holes about the border being eyelets to receive the shoe or corset laces. The large opening near the center is for the buttocks. Should the 4-inch hole prove too large, a second piece of canvas with a smaller opening may be made and pinned to the regular piece of canvas, thus making the bed adjustable for any sized buttocks.

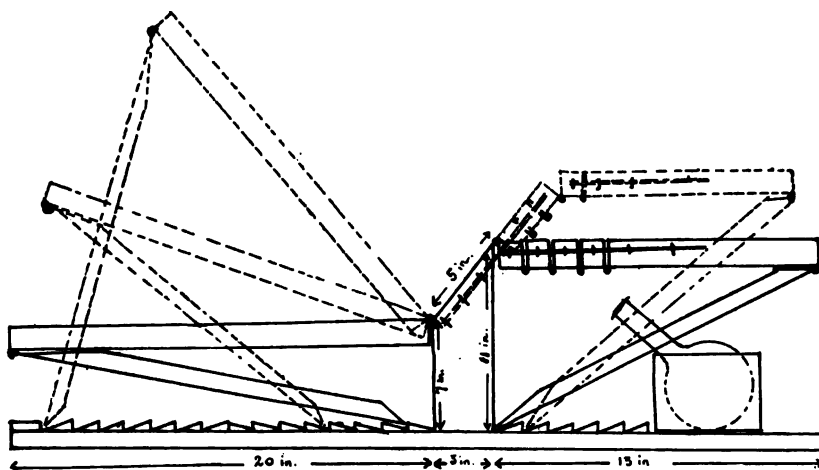


Fig. 1.—Outline of frame of metabolism bed, with dimensions, showing various positions to which it may be adjusted.

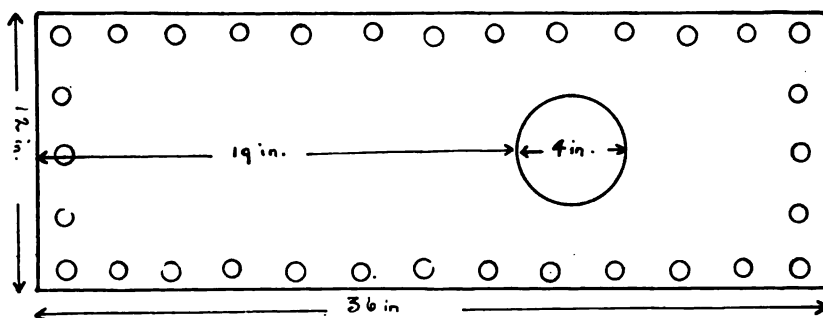


Fig. 2.—Diagram of canvas covering for frame of metabolism bed as described in the text.

Figure 3 shows pattern to be made of canton flannel or other soft cloth and attached with safety pins to the canvas shown in Figure 2. The flannel should be first placed over the canvas in such a way as to bring the round hole of the former exactly over that of the latter and then stretched smoothly and pinned. Since the flannel piece lies next the child it should be so constructed as not to chafe. The infant should wear a rather close fitting shirt with long sleeves. No other garment is neces-



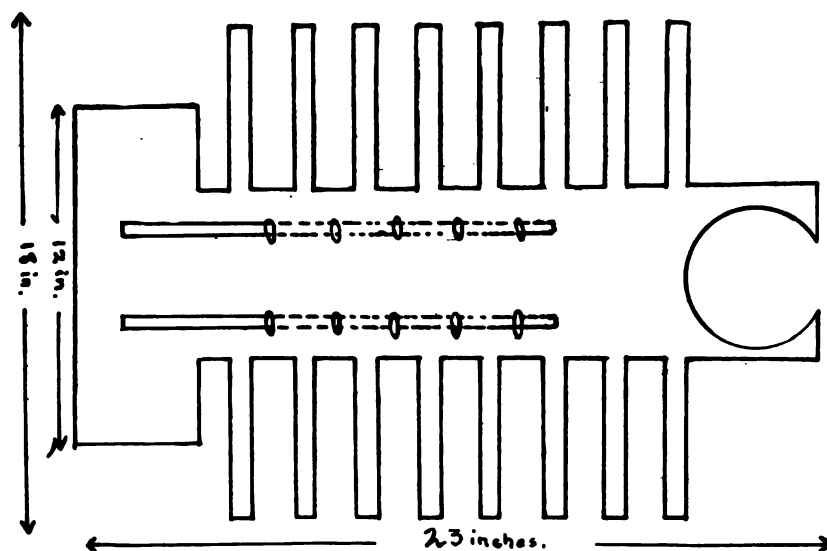


Fig. 3.—Diagram of canton flannel or other soft covering to be placed over the canvas and secured with safety pins, as described in the text. This comes in contact with the child.



Fig. 4.—Photograph of child on the frame.

sary. The subject is then placed on the frame with the buttocks in correct position. The side bands are next brought up over the abdomen and either tied or pinned, beginning at the lowest one and continuing on up until the one is reached which fits closest under the arms. If the child's body is long, more bands are used while if but an infant, three or four may suffice. After arranging the side bands those about the shoulders are then adjusted. The straps are brought through the eyelets nearest the shoulders and crossed over the chest and pinned to the side bands. If the subject be very small the bands are brought through the very lowest eyelet, whereas in an older child they are carried through the upper eyelets as shown in the drawing by the dotted and continuous lines.



Fig. 5.—Photograph of child in the horizontal position on the frame, showing the position of the receptacles for the feces and urine.

In this way children of various sizes may be placed on the frame. The bed which the author used holds equally well any sized child from the new-born to one of 5 years or more. To protect the flannel at the place where the buttocks rest a dress shield may be slipped into the opening and pinned in place.

Figure 4 is a photograph of a child on the frame. In order to clearly show details of the mechanism all blankets and other coverings have been removed. When regularly in the ward the metabolism bed rests in a crib and is so covered that one would think it merely a regular bed. Note the position of the child. As previously shown in Figure 1, it can be

placed in any posture from the horizontal to the upright. This photograph shows the sitting position. Note the shoulder and side bands in place. Attention is called to the perfect freedom of arms and legs and at the same time to the manner of lacing the canvas to the frame. The child in the photograph has been continuously five days in the frame except for the short time each morning it was taken off to be bathed. There were no pressure marks on the body and it was the universal opinion of the nurses that it was as happy and comfortable on the frame during the entire five days as in the regular ward bed. Furthermore, instead of being an additional burden to the nurses, it was considerably less care.

The child was kept perfectly warm by means of coverings placed over the bed, and when necessary, by hot water bags at the feet and back, the bag being slipped between the canvas and flannel or placed under the canvas and held in position by a pillow or folded blanket.

Figure 5 is a photograph of the child in the horizontal position. Note the position of the buttocks and the evaporating dish for the reception of the feces, and the urine flask. In the case of diarrheal stools, which are evacuated with force, deep enamel bowls should be used for the collection of the feces. These bowls are adjusted so as to fit tightly about the exposed buttocks, thus insuring perfect collection of feces even when expelled with great force. The frame is shown in proper position for noting whether collection of material is progressing satisfactorily, or for the exchange of receptacles at the end of a twenty-four-hour period. As soon as this is noted the foot of the bed is placed in the same position as in Figure 4, the head-end being adjusted to a sitting or reclining posture, dependent on whether it be play or sleep time for the child.

#### SUMMARY

Briefly to review the points brought out in the preceding description:

1. The bed is adjustable for any sized child from new-born to one 5 or 6 years of age.
2. It is adjustable for any position from horizontal to upright, which adds materially to the comfort of the child and avoids dangers incident to keeping it in one position for any length of time.
3. The child is so fastened to the frame that the buttocks remain in the same position, thus insuring complete collection of material.
4. The subject may be kept on the frame continuously for long periods without showing any pressure signs.
5. The use of the bed does not require additional work on the part of the already overburdened nurse, but on the contrary, lightens it.

6. The child can be put on or taken off the bed in about three minutes' time.

The patterns of the canvas and flannel pieces necessary for the frame, together with the measurements of the wooden parts, have been placed in the hands of Mr. Elwood Rue, a responsible cabinet maker, 219 West Twenty-Ninth Street, New York City, who will make the frame as described above for any one desiring same.

131 East Sixty-Seventh Street.

## PROGRESS IN PEDIATRICS

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### THE WASSERMANN REACTION IN SYPHILIS: A RÉSUMÉ OF CURRENT LITERATURE

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Formerly the diagnosis of congenital syphilis was entirely dependent on the clinical signs, symptoms and the history which the mother gave of previous stillbirths or miscarriages. In the last few years there have been discovered three very important methods for further examination to help in arriving at a positive diagnosis, which are as follows:

I. Microscopic diagnosis, which is based on the presence of the exciting agent — the *Treponema pallidum*.

II. The serodiagnosis, which depends on the Wassermann reaction.

III. Inoculation experiments, i. e., the injection of monkeys or rabbits with syphilitic virus.

The clinical diagnosis has been, and will naturally continue to be, the most important of all.

#### I. THE MICROSCOPIC DIAGNOSIS OF SYPHILIS

The proof of the *Treponema pallidum* being the etiologic factor in the production of syphilis depends on the following:

1. The fact that the *Treponema pallidum* has never been found in sound tissue.

2. That it is found in the tissue from

- a. Various forms of congenital syphilis.
- b. Various forms of acquired syphilis.
- c. Syphilis produced artificially in monkeys, rabbits, goats and guinea-pigs.
- d. The isolation of the *Treponema pallidum* in pure culture, completes the chain of evidence.

I. The method for the microscopic determination of the spirochetes. The serum from a primary ulcer, moist papule or chancre is collected either by a sterile platinum wire or spatula or by a sterile glass pipet.

The spirochetes may be examined living or dead.

## TECHNIC

For the detection of living spirochetes a drop of the serum is collected and placed on a clean slide with a clean cover-glass laid over it. The dark field illumination proves a much better way of studying the living form than the usual microscopic illumination. It presents the unstained specimen in a manner the reverse of the usual way; i. e., the spirochetes appear in a dark field as bright, shining, twisted, fine threads.

The specimen may be dried in the presence of the staining fluid, best sterilized Chinese ink, diluted in the proportion of 1 to 10 with distilled water, and examined with the oil immersion. The spirochetes stand out very clearly from the rest of the field, which takes the stain of the ink leaving the spirochetes as white threads.

## II. THE WASSERMANN REACTION, OR THE SERODIAGNOSIS OF SYPHILIS

In an appendix to this paper will be found a definition of the terms used (and their synonyms) in describing the Wassermann reaction. The letters in parentheses in the following paragraphs refer to paragraphs of the appendix. The method depends on the complement (B) uniting reaction first described by Bordet and Gengou in 1901. In 1905 Wassermann applied this reaction to the diagnosis of syphilis.

The reaction depends on the fact that serum from a positive syphilitic patient contains certain reaction bodies or antibodies (F) which, in the presence of a known antigen (C) from the liver of a syphilitic fetus combines with the complement. The complement being bound in this first step, does not enter into combination with the hemolytic (A-F) system, which is the indicator in the reaction, and therefore hemolysis (E) is prevented, or inhibition of hemolysis occurs, giving a positive reaction. If the serum of a normal person is brought into combination with a known syphilitic antigen, derived in the same way as above, there is *no union* with the complement, which consequently is left free to unite with the hemolytic system, the indicator again, and hemolysis does occur, giving a negative reaction.

Noguchi's<sup>1</sup> butyric acid test for increase of globulin-content in the cerebrospinal fluid is as follows: Two parts of the cerebrospinal fluid to be examined are mixed with five parts of a 10 per cent. butyric acid solution in physiologic salt solution, and are heated over a flame and boiled for a brief period. One part of a normal solution of NaOH is then added quickly to the heated mixture, and the whole boiled once more for a few seconds. The quantities which the author of this method prefers are 0.1 to 0.2 c.c. of the spinal fluid, 0.5 to 1 c.c. of the 10 per cent. butyric acid solution and 0.1 c.c. of NaOH solution. It is necessary to

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1. Noguchi: Serum Diagnosis of Syphilis, Ed. 2, p. 156.

take the precaution to employ for this test only cerebrospinal fluid entirely free from blood. Freshly drawn cerebrospinal fluid is also necessary for a satisfactory test. The presence of an increased content of protein in the cerebrospinal fluid is indicated by the appearance of a granular or floccular precipitate, which gradually settles to the bottom of the tube, beneath a clear supernatant fluid. The velocity and intensity of the reaction varies according to the quantity of the protein contained in a given specimen. The granular precipitate appears within a few minutes in a specimen containing a considerable increase in protein, while one to two hours may be required to obtain a distinct reaction in specimens weaker in proteins.

Normal cerebrospinal fluid gives with the butyric acid test a slight opalescence and sometimes a marked turbidity, but the granular precipitate does not occur at all or occurs only after several hours or even after twenty-four hours.

The Nonne-Apelt method for testing globulin in cerebrospinal fluid is considered by the German workers to be more delicate, and, having the necessary testing solutions, it is easily carried out. It is as follows:

1. A saturated solution of ammonia sulphuric (Wurck, Darmstadt), made up as follows: 1.85 gm. to 100 c.c. of distilled water is boiled in an Erlenmeyer flask until the solution no longer dissolves; allow this to cool; filter. This is the test solution. To test for the presence of globulin take 1 c.c. of the test solution and 1 c.c. of fresh cerebrospinal fluid. Allow this mixture to stand in a cold place for three minutes. Interpretation of this globulin reaction is positive if, after three minutes, clouding or opalescence appears in the mixture. These reactions are found frequently in syphilitic and parasyphilitic cases even where there is no disease of the central nervous system, though of course they are more positive in cerebrospinal syphilis and tabes dorsalis and syphilitic dementias. They are, however, also just as constantly found in certain non-syphilitic conditions which of course would have to be ruled out before a positive reaction could be taken to indicate syphilis. They are positive in *all inflammatory conditions of the meninges*, such as those caused by the following organisms: *Diplococcus intracellularis*, pneumococcus, influenza bacillus, tubercle bacillus and the virus of poliomyelitis; also during acute febrile manifestations, as pneumonia, typhoid, septicemia, acute anemias.

The reaction simply indicates an inflammatory reaction of the meninges and therefore has nothing of a specific nature in its results as the Wassermann reaction has.

The Wassermann reaction has called into question two didactically accepted laws:

1. The so-called Colles law, according to which the mothers of syphilitic children are immune against syphilis; that is, are sound.

2. The Profeta law, according to which the children of syphilitic mothers are immune against syphilis. It is a well-accepted fact that syphilitic children have often no manifestation or external symptoms of lues; even the well-known Hutchinson's triad is comparatively rare. There is often only a simple anemia or a slight nervous condition.

#### OPINIONS ON COLLES' AND PROFETA'S LAWS

Muller found that with the blood of wives of syphilitic husbands, where the wife had repeated abortions and premature births, the results were usually negative and their offspring also gave negative reactions.

Knopfmacher and Lehndroffer<sup>2</sup> examined thirty-two apparently healthy mothers of syphilitic children and obtained positive reactions in eighteen.

Halberstadler, Muller and Reiche found that the reaction may be negative with children of syphilitic mothers and vice versa, while Boas and Thomsen assert that the reactions can develop later in children whose bloods give a negative reaction at the time of birth. They all agree that the negative reaction in these children or mothers is largely due to the latency of the disease, but is not a sign of immunity against the disease. Thus, while the mothers of a syphilitic infant may present no sign of syphilis, yet the examination of the blood of the mother gives a positive reaction in at least half the number of cases examined.

The study of congenital syphilis by the Wassermann reaction has added much valuable information to our didactic knowledge of this condition. Baish,<sup>3</sup> in an extensive study of 140 mothers who had miscarriages or luetic children, has elucidated some points in the transmission of syphilis. Of these, twenty-four mothers gave a negative reaction and the dead fetuses showed no spirochetes, while 102 mothers gave a positive reaction and gave birth to fetuses or children with congenital lues, in whom the *Treponema pallidum* was demonstrated. Of these 102 mothers, twenty-seven had evidence of syphilis, while seventy-two were free from such evidence. With these women the positive reaction may have been due either to a latent syphilis, the women being spirochete carriers, or the complement fixing bodies may have been formed in the fetuses and have filtered through the placenta into the maternal circulation. Baish found *Treponema pallidum* not only in the placenta, but in the maternal portion of the decidua, so he concludes that the mothers were actually

2. Knopfmacher and Lehndroffer: Das Colles'sche Gesetz, Med. klin., 1909, v, 1906; Das Colles'sche Gesetz und neuen syphilisforschungen, Jahrb. f. Kinderh., 1910, lxxi, 156.

3. Baish, K.: München. med. Wchnschr., lvi, 1929.



infected. He showed that the intensity of the reaction in the mothers did not diminish after the delivery of the child, as would be expected were the antibodies formed in the child and filtered through the placenta. At times the blood of the mother and the child gave different reactions; this would not be the case if the immune bodies filtered through the placenta.

In twelve mothers with a negative reaction the fetus and placenta showed spirochetes, a finding which proves that they may be present without exciting the formation of the complement-fixing bodies; but the evidence of spirochetes in the placenta of all the positively reacting cases leads Baish to the conclusions that this fixing substance is always dependent on the presence of spirochetes somewhere in the body.

Swift examined fourteen cases of congenital lues; twelve of these gave a positive reaction. The two negative reactions were obtained in women who had undergone years of mercurial treatment. In ten women who had borne children with congenital syphilis, or who had had syphilitic miscarriages, nine gave a positive reaction. None of these women recalled any evidences of syphilis before labor; later five of them presented tertiary manifestations; four remained free from all clinical evidences of the disease, but only one of these four gave a negative reaction.

I examined twenty mothers with syphilitic children with only one negative reaction, and ten women with babies in whom a positive clinical diagnosis could not be accurately made, with seven positive reactions. The three negative cases have not shown any more definite symptoms than when first seen and their babies have thrived without any specific treatment. Only six of these thirty mothers gave any history of specific lesions or had any evidence of lues at the time the reactions were done.

The importance of the reaction in wet-nurses needs especial attention now that their use is being so widely acknowledged in difficult feeding cases or in cases in which breast-feeding is desired during the first few months of life. The writer has done reactions in twenty-six cases of wet-nurses with three positive reactions. All three of these cases had no signs of lues from their previous histories; all were primiparas (mostly illegitimate births), and as far as their physical examinations went were apparently free from any specific taint and at the time of the reaction their children were all normal.

With all this evidence it would seem that the period of immunity, defined by Colles' law, is really a period of latent syphilis, as shown by reactions. A positive reaction in a high percentage of sound children from clinically syphilitic mothers, similarly shows that their immunity defined by Profeta's law is only latency. It is well known that many of these so-called immune mothers and children later present evidence of syphilis. It should be made a rule to treat any such apparently sound

mothers or children who give a positive reaction as though they presented active evidences of the disease, and to rule out any wet-nurse that reacts positively from nursing any but known luetic babies.

Ravait, Breton and Petit<sup>4</sup> obtained positive reactions in 30 to 40 per cent. of cases of epilepsy, idiocy and imbecility.

Verches described a congenital syphilis of the lung in the form of a white pneumonia. It is not of frequent occurrence, though it can be recognized. It is usually fatal.<sup>5</sup>

That the syphilitic virus often attacks with unusual severity the heart and blood-vessels is only lately being fully appreciated. The arteries of the arch of Willis are most often attacked of the small arteries. An acute gummatous endarteritis of some of the large arteries in the brain as well as of the aorta are now positively and not infrequently recognized; obliterative endarteritis of the small blood-vessels of the brain, and especially of the coronaries, is met with. Fibrous myocarditis with anginal attacks are met with in the young. Gumma may occur in the heart wall. It is estimated that from 20 to 80 per cent. of aneurysms are due to syphilitic disease of the blood-vessels.<sup>6</sup>

Sachs<sup>7</sup> has pointed out that any method which will aid in differentiating between a central gliosis and a specific central myelitis, between a malignant brain tumor and a gumma, should be most welcome. In syphilitic conditions of the bones found in children, such as periostitis, gumma and osteomyelitis, the test has proved positive more often than in any other class of cases. Swift<sup>8</sup> examined seventeen such cases with only one negative result and as this case had been under treatment for six months with but little effect, lues could be fairly well eliminated, as there had been little or no effect from the therapeutic treatment.

#### APPENDIX

A. *Amboceptor* (Noguchi, ed. 2, p. 179, Glossary).—Introduced by Ehrlich; is synonymous with *Fixateur* of Metchnikoff. *Substance sensibilisatrice* of Bordet, Preparator of Max Gruber, and Copula of Prof. Th. Müller. Amboceptor is one of the two active principles necessary to cause hemolysis, bacteriolysis, or any other cytotoxicity caused by serum, the other active principle being complement. Amboceptor retains its activity after the serum is heated to from 55 to 56 C. for thirty minutes, while complement is destroyed at that temperature. Amboceptor, as well as complement, is present in the coagulable protein fraction of serum. Amboceptor may be present in any normal serum, and can be produced in

4. Ravait, Breton and Petit: *Recherches sur la reaction de Wassermann chez 400 aliènes*, *compt. rend Soc. de biol.*, Feb. 29, 1908; *Rev. de méd.*, 1908, xxviii, 840.

5. Billings, Frank: *Jour. Am. Med. Assn.*, Nov. 18, 1911, p. 1653.

6. Collins, J., and Sachs, B.: *Am. Jour. Med. Sc.*, 1901, cxxi, 344; Citron. J.: *Berl. klin. Wehnschr.*, 1908, xlv, 2142; Donath: *Berl. klin. Wehnschr.*, 1909, xlv, 2015.

7. Sachs, B.: *Jour. A. M. A.*, 1909, lii, 929.

8. Swift, H. F.: *Cleveland Med. Jour.*, May, 1910.

the serum of an animal by injecting repeatedly the cell for which it has no amboceptor. The amboceptor normally present is called natural amboceptor and that which is produced by means of repeated injections of foreign cells is called immune amboceptor. The amboceptor capable of causing hemolysis (in presence of complement, of course) is called hemolytic amboceptor, while that which is capable of dissolving bacteria is called bacteriolytic amboceptor. A few writers use the simple terms hemolysin or bacteriolysin instead of hemolytic or bacteriolytic amboceptor. Amboceptors are capable of producing anti-amboceptors when injected into a susceptible animal.

B. *Complement* (Noguchi, p. 181, Glossary).—Introduced by Ehrlich; is synonymous with Metchnikoff's cytase and Bordet's alexin. By the term complement one understands one of the two active principles concerned in hemolysis, bacteriolysis, and other instances of serum cytolysis. The other principle is called amboceptor, which is incapable of causing dissolution of cells without the first; hence the term complement is applied to it. Complement is normally present in all sera freshly drawn from the body, but disappears gradually on standing or is completely destroyed at from 55 to 56 C. in about thirty minutes. Complement of one species is not identical in its action with that of other species.

C. *Antigens* (Noguchi, p. 180).—A general term applied to a group of substances capable of producing specific antibodies administered once or repeatedly, usually by injection, to a suitable animal. For example, bacteria, blood corpuscles, and certain somatic cells are antigens because they produce specific antibodies called amboceptors and agglutinins. Blood serum, milk or bacterial extracts are also antigens, because they produce antibodies. On the other hand, most inorganic or organic substances with definite chemical structure are not antigens, because their introduction is not followed by the formation of antagonistic substances (antibodies) in the body. Repeated administrations of various alkaloids render the organism gradually more resistant to their effect, but do not produce antibodies; hence these alkaloids are not antigens. Diphtheria toxin, tetanus toxin, ricin, abrin, snake venoms, are antigens and their injections are followed by specific antitoxins, as is well known.

D. *Complement Deviation* (Noguchi, p. 181).—Synonymous with deflection; originates from a German term, Ablenkung, introduced by Neisser. Complement deviation is identical with Komplementablenkung of the Germans, and fixation of alexin of the French. By the deviation of complement one understands that complement is fixed by the antigen-antibody combination and is made unavailable for a second set of antigen-antibody combination to complete a reaction in which complement is essential. This second set may be a hemolytic or a bacteriolytic system.

E. *Hemolysis* (Noguchi, p. 182).—Dissolution of blood-corpuscles by various forces, setting the hemoglobin free into the medium in which the corpuscles are suspended. Distilled water, freezing and thawing, temperature of about 55 C. for thirty minutes, etc., are physical agents which cause hemolysis. Acids, alkalies, and certain salts can cause hemolysis in proper concentrations. Of these chemicals may be mentioned most organic acids, mineral acids, all alkalies, bile salts, bichlorid of mercury, soaps. Of biologic origin may be mentioned certain glycosides such as saponin, solanin, etc., certain bacterial cultures, such as those of staphylococcus, vibrios, megatherium, tetanus bacillus, etc.; certain animal venoms such as those of snakes, bees, spiders, etc. The hemolytic process caused by these different agents is different according to the nature of the hemolytic forces, but they attack the corpuscles more or less directly. Hemolysis by serum is, however, somewhat different from that caused by the various forces just mentioned. Thus, hemolysis by fresh alien serum is caused by two distinct groups of substances both contained in blood serum. One is called complement and the other amboceptor. The one is inactive without the other. Serum hemolysis forms the basis of many interesting phenomena, the serum diagnosis of syphilis being one of these.

F. *Antibodies* (Noguchi, p. 180).—A general term applied to a group of reaction products arising from single or repeated administrations of antigens to a suitable animal. Immune body is a synonym of antibody. Among antibodies we may enumerate hemolytic amboceptors, bacteriolytic amboceptors, other cytolytic amboceptors, precipitins, agglutinins, antitoxins, antivenins, antiricin, antiabrin, etc. Antibodies possess specific affinity for the antigens which are used for their production. Certain antibodies such as agglutinins, amboceptors, antitoxins, or antihemolysins may be normally present in certain sera in small amount. A group of antibodies is capable of producing antibodies when injected into another animal, thus forming anti-antibodies.

## INDEX OF CURRENT PEDIATRIC LITERATURE

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### ANATOMY, PHYSIOLOGY AND HYGIENE

- Program for Sex Instruction. I. S. Wile.  
Arch. Pediat., February, 1912.
- Prophylactic Value of Instruction of Children in Elements of Physiology of Sex.  
C. A. Pfender.  
Texas Jour. Med., February, 1912.
- What a Father Should Tell His Son. I. S. Wile.  
New York Med. Jour., March 9, 1912.
- What a Mother Should Tell Her Child. M. S. Macy.  
New York Med. Jour., March 9, 1912.
- Blackboard Evil, Remedy; Copy-Book Evil, Remedy. J. N. Rhoads.  
Pennsylvania Med. Jour., February, 1912.
- Our Duty to School Children. A. M. Heron.  
Jour. Med. Soc. New Jersey, February, 1912.
- Report of Committee to Investigate Teaching of Hygiene in Public Schools. H. C. Putnam.  
Bull. Am. Acad. Med., February, 1912.
- The Poor School for the Poor Boy; Is It Necessary? F. A. Carmichael.  
Jour. Kansas Med. Soc., February, 1912.
- Vaccine Virus and Results of Vaccination in Public Schools of St. Louis, 1912.  
G. Dock and D. L. Harris.  
Interstate Med. Jour., February, 1912.
- Responsibility of General Practitioner to Child with Speech Defect. H. Horn.  
California Jour. Med., February, 1912.
- The Treatment of Occluded "S." E. W. Scripture.  
Jour. Am. Med. Assn., March 9, 1912, p. 695.
- Infant Welfare Organizations at Nice. (Création d'une Goutte de Lait par la Société protectrice de l'enfance de Nice.) A. Balestre and L. d'Oelsnitz.  
Arch. méd. d. enf., February, 1912.
- A Plea for Mongol. T. E. Green.  
Australian Med. Gaz., Dec. 30, 1911.

### PATHOLOGY AND BACTERIOLOGY

- Hyper- and Hypothyroid Gland in Childhood. C. F. Tenney.  
Ohio Med. Jour., February, 1912.
- Normal Involution of the Thymus. C. Barbano.  
Virchow's Arch. f. path. Anat., January, 1912.
- Occurrence of Fat in the Thymus Parenchyma. (Om förekomsten af fett eller fettliknande substanser i thymusparenkymet.) R. Holmström.  
Uppsala Läkaref. Förh., 1912, xvii, No. 3.
- Pathologic Involution of the Thymus. (Thymusstudien. I. Auftreten von Fett in der Thymus.) K. Hart.  
Virchow's Arch. f. path. Anat., January, 1912.
- Disease of the Adrenals and Appendix in Connection with Fecal Obstruction. (Ueber den Zusammenhang von Nebennieren- und Appendixerkrankungen mit schweren Kotstauungen.) A. Brosch.  
Virchow's Arch. f. path. Anat., January, 1912.
- Diagnostic Significance of Rigidity of Neck Muscles in Children. L. Kerr.  
Am. Jour. Obst., February, 1912.

- Pseudomuscular Hypertrophy. M. G. Burris.  
Canadian Med. Assn. Jour., January, 1912.
- Congenital Myatonia. (Zur Klinik und Pathologie der Myatonia congenita—Oppenheim.) O. Marburg.  
Arb. a. d. interacad. Zentralin. f. Hirnforschung, 1912, xix, No. 2.
- Anaphylaxis as Explanation of Sudden Death after Burns. (Ursachen des Verbrennungstodes.) M. Heyde.  
Med. Klin., Feb. 18, 1912.
- Characteristics of Prehistoric Skeletons in Cretins. (Neandertalmerkmale bei Kretinen.) Fiukbeiner.  
Ztschr. f. Kinderh., January, 1912.
- Large Angiomas; Two Cases. (Zur Pathologie der Angiome.) G. E. Konjetzny.  
München. med. Wehnschr., Jan. 30, 1912.
- Symmetrical Gangrene in Boy of 3. (Cas très grave de maladie de Raynaud chez un enfant de trois ans.) G. Variot and Morance.  
Bull. de la Soc. de Pédiat., January, 1912.

### METABOLISM AND NUTRITION

- Breast Nursing Propaganda. (Poliklinische Beobachtungen aus der Stillpropaganda.) E. Mayerhofer.  
Wien. klin. Wehnschr., Feb. 15, 1912.
- Prevention of Infant Mortality by Breast-Feeding. W. H. Davis.  
Boston Med. and Surg. Jour., Feb. 15, 1912.
- Card for Rapid Calculation of Milk Modifications. J. H. Young.  
Boston Med. and Surg. Jour., March 7, 1912.
- Chemical Composition of Human Milk. II. (Die chemische Zusammensetzung der Frauenmilch auf Grund neuer Analysen.) E. Schloss.  
Monatschr. f. Kinderh., 1911, x, No. 10.
- Intoxication from Milk and Tolerance for Desiccated Milk. (Intoxication par le lait liquide et tolérance pour le lait sec.) M. Nageotte-Wilbouchevitch.  
Bull. de la Soc. de pédiat., January, 1912.
- Preserved Human Milk for Infant Feeding. (Praktische Erfolge der Ernährung mit konservierter Frauenmilch.—Bericht über 100 Fälle.) E. Mayerhofer and E. Pribram.  
Ztschr. f. Kinderh., January, 1912.
- Rapid and Simple Method for Calculating Caloric Value of Percentage Mixtures. F. Fraley.  
Arch. Pediat., February, 1912.
- Silicic Acid in Milk Sterilized in Glass Bottles. (Der Uebergang von Kieselsäure in die Milch beim Sterilisieren in Glasflaschen.) H. Schultz.  
München. med. Wehnschr., Feb. 13, 1912.
- Comparative Caloric Value of Various Foods Used in Infancy and Early Childhood. C. B. Farr.  
Arch. Pediat., February, 1912.
- Nutrition in Infancy. A. P. Crain.  
New Orleans Med. and Surg. Jour., March, 1912.
- Underfed School Children. (Hungernde Kinder?) M. Pfaundler.  
München. med. Wehnschr., Jan. 30, 1912.
- Infantile Scorbutus. W. Weston.  
Jour. S. Carolina Med. Assn., February, 1912.
- Action of Salts on Infant's Organism. (Die Wirkung der Salze auf den Säuglingsorganismus auf Grund früherer und neuerlicher Untersuchungen.) E. Schloss.  
Ztschr. f. Kinderh., January, 1912.
- Growth and Osmotic Pressure in Young Dogs. II. (Wachstum und osmotischer Druck bei jungen Hunden.) P. Schultz.  
Ztschr. f. Kinderh., January, 1912.

- Volume and Specific Gravity of Living Infants. (Körpervolumen und spezifisches Gewicht von Säuglingen.) O. Kastner. (Körpervolum und Körperdichtebestimmung am lebenden Säugling.) M. Pfaundler.  
Ztschr. f. Kinderh., January, 1912.

# DISEASES OF THE NEWLY-BORN

- Case of Spontaneous Umbilical Hemorrhage in Two-Weeks-Old Baby. H. C. Dodge.  
Denver Med. Times and Utah Med. Jour., February, 1912.
- Hemorrhagic Disease of Newborn. S. C. Spencer.  
Mississippi Med. Month., February, 1912.
- Case of Congenital Gangrene of Right Fore-Arm, with Successful Amputation, in Infant Five Days Old. R. Winslow.  
South. Med. Jour., February, 1912.
- Erysipelas in New-Born Infant. G. T. Welch.  
Jour. Med. Soc. New Jersey, February, 1912.
- Mortality of the Prematurely Born in Relation to the Causes of the Premature Delivery. (La mortalité des prématurés dans ses relations avec les causes de la prématurité.) Plauchu.  
Arch. men. d'obstet. et de gynec., January, 1912.
- Temperature of the Prematurely Born. (Zur Lehre von der Temperatur der Frühgeborenen.) F. Masay.  
Jahrb. f. Kinderh., February, 1912.

# ACUTE INFECTIOUS DISEASES

- Acute Poliomyelitis with Unusual Manifestations. M. Greenwald.  
New York Med. Jour., Feb. 17, 1912.
- Anterior Poliomyelitis. M. B. Hodskins.  
Vermont. Med. Month., February, 1912.
- Epidemic Poliomyelitis and Its Treatment. (Den Heine-Medin'ske Sygdom og dens Behandling.) H. C. Sloman.  
Ugesk. f. Læger., Feb. 8, 1912.
- Experimental Poliomyelitis. F. E. Batten.  
Lancet, London, Feb. 17, 1912.
- Infantile Paralysis. F. F. Bowyer.  
Jour. Med. Soc. New Jersey, February, 1912.
- Infantile Paralysis, or Acute Anterior Poliomyelitis. W. D. Hoskins.  
Jour. Indiana Med. Assn., February, 1912.
- Poliomyelitis. L. B. Russell.  
Illinois Med. Jour., February, 1912.
- Treatment of Infantile Paralysis. H. J. Bogardus.  
Jour. Med. Soc. New Jersey, February, 1912.
- Study of Cerebrospinal Fluid and Blood in Acute Poliomyelitis. G. Draper and F. W. Peabody.  
Am. Jour. Dis. Child., March, 1912.
- Symptomatology and Diagnosis of Infantile Paralysis. C. H. Finke.  
Jour. Med. Soc. New Jersey, February, 1912.
- Epidemic Cerebrospinal Meningitis. H. S. Millar.  
Dublin Jour. Med. Sc., February, 1912.
- Epidemic Cerebrospinal Meningitis. E. M. Dupaquier.  
New Orleans Med. and Surg. Jour., March, 1912.
- Modern View of Meningitis. H. M. McClanahan.  
West Med. Rev., February, 1912.
- Pneumographic Study of Respiratory Irregularities in Meningitis. L. A. Conner and R. G. Stillman.  
Arch. Int. Med., February, 1912.

- Present Status of Treatment of Suppurative Meningitis. (Ueber den gegenwärtigen Stand der Therapie der eitrigen Meningitis.) F. Henke.  
Med. Klin., Feb. 25, 1912.
- Prophylaxis of Cerebrospinal Meningitis, with Some Observations as to Carriers.  
Howard D. King.  
Jour. Am. Med. Assn., Feb. 10, 1912, p. 403.
- Treatment of Cerebrospinal Meningitis. (Contribution à l'étude du traitement de la meningite cerebrospinale.) Cantas and A. Netter.  
Bull. de l'Acad. de méd., Paris, Jan. 30, 1912.
- Bacteriologic Diagnosis of Diphtheria. (Zur bakteriologischen Diagnose der Diphtherie.) Schopohl.  
Deutsch. med. Wchnschr., Feb. 22, 1912.
- Contribution to Passive Immunization in Diphtheria of Upper Respiratory Organs.  
H. L. Wagner.  
Ann. Otol., Rhin. and Laryng., December, 1911.
- Diagnosis and Treatment of Diphtheria. J. C. Anderson.  
Texas Jour. Med., February, 1912.
- Diphtheroid Bacilli of Penis; Report of Two Cases of Diphtheria Following Circumcision. J. A. Kolmer.  
Arch. Pediat., February, 1912.
- Role of Animal Experimentation in the Discoveries Leading to Our Present Knowledge of the Etiology, Prevention and Cure of Diphtheria. W. H. Park.  
Jour. Am. Med. Assn., Feb. 17, 1912, p. 453.
- Relation of Streptococci to Scarlet Fever With Active Immunization by Means of Streptococcic Bacterins. J. A. Kolmer.  
Pennsylvania Med. Jour., February, 1912.
- Scarlet Fever. (Ueber Scharlach.) K. Preisich.  
Jahrb. f. Kinderh., February, 1912.
- Streptococcus Vaccines in Scarlet Fever Prophylaxis. W. H. Watters.  
Jour. Am. Med. Assn., Feb. 24, 1912, p. 546.
- Study of Streptococcus Antibodies in Scarlet Fever with Special Reference to Complement Fixation Reactions. J. A. Kolmer.  
Arch. Int. Med., February, 1912.
- Observations on Nervous Manifestations in Rheumatism of Childhood. F. J. Poynton.  
Brit. Jour. Child. Dis., February, 1912.
- Series of Manifestations of Acute Rheumatism in Boy of Ten. R. B. Ness.  
Brit. Jour. Child. Dis., February, 1912.
- Ascending Peritonitis in Little Girls. (Ueber Peritonitis purulenta ascendens.) G. Mertens.  
München. med. Wchnschr., Jan. 30, 1912.
- Cholera Infantum. M. J. Tanquary.  
Jour. Kansas Med. Soc., February, 1912.
- Convulsive Tendencies During and After Encephalitis in Children. W. P. Lucas and E. E. Southard.  
Boston Med. and Surg. Jour., Feb. 29, 1912.
- Huntington's Chorea. L. C. Lewis.  
New York State Jour. Med., February, 1912.
- School Closure in Measles. A. B. Raffle.  
Lancet, London, Feb. 3, 1912.
- Malaria in Children. (La malaria nell'infanzia.) V. Fusco.  
Gazz. d. osp., Feb. 18, 1912.
- Vitiligo and Chorea. K. Malinckrodt.  
Monatschr. f. Kinderh., 1911, x, No. 10.
- Whooping-Cough. (Zur Ätiologie und Pathologie des Keuchhustens.) E. Döbeli.  
Cor.-Bl. f. schweiz. Aerzte, Feb. 1, 1912.



## TUBERCULOSIS AND SYPHILIS

- Differential Diagnosis of Congenital Syphilis and Tuberculosis of Bones and Joints. C. G. Cumston.  
Arch. Diagnosis, January, 1912.
- Hydrocephalus and Syphilis. (Hydrocephalus und Lues.) W. Knöpfelmacher and W. Schwalbe.  
Ztschr. f. Kinderh., January, 1912.
- Inherited Syphilis of the Nervous System. (Quelques faits d'hérédosyphilis du système nerveux.) H. Barbier and Gassier.  
Bull. de la Soc. de pédiat., January, 1912.
- Localization of *Spirochæta Pallida* in the Heart-Muscle in Congenital Syphilis in the Absence of Histologic Lesions or Spirochetes Elsewhere in the Body. A. S. Warthin.  
Jour. Am. Med. Assn., March 9, 1912, p. 689.
- Parasyphilitic Disease in Infancy. R. Koenigstein.  
Med. Press and Cir., Jan. 17, 1912.
- Salvarsan in Treatment of Inherited Syphilis in Infants. (Klinische Beobachtungen bei der Salvarsanbehandlung syphilitischer Säuglinge.) C. T. Noeggerath.  
Jahrb. f. Kinderh., February, 1912.
- Syphilitic Leptomeningitis in Infants. (Zur Kenntnis derluetischen Leptomeningitis beim Säugling.) E. Rach.  
Jahrb. f. Kinderh., February, 1912.
- The Chest Measure and Tuberculosis. (Tour de poitrine et poitrinaires.) H. Marcou.  
Arch. gen. de méd., January, 1912.
- Diagnosis of Thoracic Gland Tuberculosis During Childhood. L. C. Ager.  
Arch. Diagnosis, January, 1912.
- Dispensary Tuberculin Treatment of Scrofula and Tuberculosis in Children. (Versuch einer poliklinischen Tuberculinbehandlung der kindlichen Skrofulose und Tuberkulose.) H. Wittich.  
Jahrb. f. Kinderh., February, 1912.
- The Early Recognition of Tuberculosis in Childhood. W. C. Hollopeter.  
Pediat., February, 1912.
- Intrathoracic Tuberculosis in Infancy and Childhood, Based on a Study of 125 Cases. L. C. Ager.  
Am. Jour. Obst., February, 1912.
- Prognosis of Tuberculosis in Infants. (Prognose der Säuglingstuberkulose.) H. Hahn.  
Monatschr. f. Kinderh., 1911, x, No. 10.
- Tuberculin Treatment of Latent Tuberculosis and Incipient Phthisis in Children. (Das Endotin—Tuberculin. purum—bei latenter Tuberkulose und Phthisis incipiens im Alter von 10 Jahren an.) D. Kurdjumoff.  
Beitr. z. Klin. d. Tuberk., 1912, xxii, No. 1.
- Tuberculosis in Childhood from Clinical Standpoint. S. G. Wilson.  
New Orleans Med. and Surg. Jour., February, 1912.
- Tuberculosis of the Hilus of the Lung in Children. (Die Hilustuberkulose des Kindes im Röntgenbilde.) E. Sluka.  
Wien. klin. Wchnschr., Feb. 15, 1912.
- Tuberculosis of Mesenteric Glands in Children: Its Nature and Treatment. E. M. Corner.  
Lancet, London, Feb. 17, 1912.
- Unfavorable Experiences with Spengler's I. K. Method in Ten Cases of Tuberculosis. (Erfahrungen mit C. Spengler's I. K.) O. Baer.  
Berlin. klin. Wchnschr., Jan. 29, 1912.

### DIGESTIVE SYSTEM

- Atrophy of Infants. A. Czerny.  
Am. Jour. Dis. Child., March, 1912.
- Cases of Imperforate Anus and Malformed Rectum. C. P. Farnsworth.  
Med. Rec., New York, March 9, 1912.
- Cause and Treatment of Summer Diarrhea in Children. A. J. Wood.  
Australian Med. Gaz., Dec. 30, 1911.
- Congenital Idiopathic Dilatation of Colon, Hirschsprung's Disease. J. F. Critchlow.  
Northwest Med., February, 1912.
- Dental Hygiene of Childhood. G. Thomson.  
Med. Press and Circ., 1912, xciii, 183.
- Digestive Disturbances in Infants and Their Treatment. (Die Ernährungsstörungen im Säuglingsalter und deren Behandlung.) E. Wieland.  
Cor.-Bl. f. schweiz. Aerzte, Feb. 10, 1912.
- Diverticulum of Meckel Opening into the Umbilicus. (Persistance du diverticule de Meckel ouvert à l'ombilic.) E. Kirmisson.  
Bull. de l'acad. de méd., Paris, Feb. 20, 1912.
- Enterectomy Under Spinal Anesthesia for Acute Intestinal Obstruction in Infant Twenty-Four Hours Old; Survival for One Month. G. E. Waugh.  
Lancet, London, Feb. 17, 1912.
- Foreign Bodies in Esophagus; Two Cases. (Corps étranger dans L'œsophage.) H. Abrand.  
Bull. de la Soc. de pédiat., January, 1912.
- Gastrogenic Diarrhea. C. D. Aaron.  
Arch. Diagnosis, January, 1912.
- Intussusception. J. C. King.  
South. California Prac., February, 1912.
- A Study of Children with Reference to Enteroptosis. Richard R. Smith.  
Jour. Am. Med. Assn., Feb. 10, 1912, p. 385.
- Use of Intestinal Antiseptics in Childhood. A. Hand.  
Arch. Pediat., February, 1912.
- Use of a Simple Duodenal Catheter in Diagnosis and Treatment of Certain Cases of Vomiting in Infants. A. F. Hess.  
Am. Jour. Dis. Child., March, 1912.
- Visible Gastric Peristalsis in Infants. (Ueber sichtbare Magenperistaltik beim Säugling.) T. Hoffa.  
Monatschr. f. Kinderh., 1911, x, No. 10.

### RESPIRATORY SYSTEM

- Bronchopneumonia in Infancy and Childhood. L. Fischer.  
Pediat., February, 1912.
- Case of Multiple Foreign Bodies in Smaller Bronchi. F. E. Hopkins.  
Ann. Otol., Rhin. and Laryng., December, 1911.
- Disturbances and Findings with Tracheobronchial Lymphadenitis in Young Children. (Caractères des troubles respiratoires et des images radioscopiques dans l'adénopathie trachéo-bronchique de la première enfance.) L. d'Oelsnitz.  
Rev. mens. d. gynéc., et d. pédiat., January, 1912.
- Primary Pneumonia in Childhood. R. Hutchison.  
Clinical Journal, 1912 xxxix, 289.
- Removal of Foreign Body from the Right Bronchus. Frank C. Todd.  
Jour. Am. Med. Assn., March 9, 1912, p. 692.
- Tacks and Nails in the Air-Passages; Bronchoscopy. E. Fletcher Ingals.  
Jour. Am. Med. Assn., Feb. 17, 1912, p. 467.

# BLOOD AND CIRCULATORY SYSTEM

- Arhythmia in Children. (Om arytmi, s skildt hos barn.) R. Friberger.  
Upsala L karef. F rh., 1912, xvii, No. 3.
- Case of Patent Ductus Arteriosus Botalli. A. G. Sison.  
Bull. Manila Med. Soc., December, 1911.
- Diphtheritic Changes in the Heart Muscle. (Ueber die Ver nderungen der Herzmuskulatur vor allem des Atrioventrikularbundsels bei Diphtherie; zugleich ein Beitrag zur Frage der Selbst ndigkeit des B ndels.) T. Tanaka.  
Virchow's Arch. f. path. Anat., January, 1912.
- Embryonal Cells Behave like Cancer Cells in Respect to Blood from the Umbilicus and Retroplacental Serum. (Verhalten embryonaler Zellen gegen ber Nabelblut und Retroplazentarserum.) R. Kraus, K. Ishiwara and J. Winternitz.  
Deutsch. med. Wchnschr., Feb. 15, 1912.
- Normal Human Blood-Serum Injections in Melena Neonatorum and Other Conditions. J. E. Welch.  
Therap. Gaz., February, 1912.
- Operative Treatment of Adhesive Pericarditis. (Le traitement chirurgical de la m diastino-p ricardite adh sive.) A. Rives.  
Arch. gen. de chir., January, 1912.
- Purulent Pericarditis in Children. (De la p ricardite purulente chez les enfants; p ricardite traumatique.) V. Imervol.  
Arch. m d. des enf., February, 1912.
- Simulated Ileus and Pneumococcus Septicemia. (Pseudo-occlusion intestinale et septic mie   pneumocoque.) H. Triboulet and S. I. De Long.  
Bull. de la Soc. de p diat., January, 1912.
- Treatment of Melena Neonatorum by Human Blood Serum. W. R. Nicholson.  
Therap. Gaz., February, 1912.
- Vasoconstricting Substance in Infants' Blood-Serum. (Ueber gef  ssverengernde Substanzen in S uglingsblutserum.) S. Samelson.  
Ztschr. f. Kinderh., January, 1912.
- Venous Hums in Children. H. R. M. Landis and I. Kaufman.  
Arch. Pediat., February, 1912.

# NERVOUS SYSTEM

- Delirium in Children. (Les d lires chez les enfants.) J. Comby.  
Arch. m d. d. enf., February, 1912.
- Lumbar Puncture in Diagnosis of Disease of the Brain and Spinal Cord. (Bedeutung der Lumbelpunktion f r die Diagnose von Gehirn- und R ckenmarkskrankheiten.) Stertz.  
Med. klin., Jan. 28, 1912.
- Prognosis of Epilepsy in Children. (Zur Prognose der Epilepsie im Kindesalter.) J. Zappert.  
Med. Klin., Feb. 11, 1912.
- The Spinal Ganglia in Children. (Die Spinalganglien im Kindesalter.) J. Zappert.  
Arb. a. d. interacad. Zentrallin. f. Hirnforschung, 1912, xix, No. 2.

# GENITO-URINARY SYSTEM

- Acute Scarlatinal Nephritis in Children. H. B. Cheffield.  
Pediat., February, 1912.
- Case of Acute Hemorrhagic Nephritis in Girl of 10 After Impetiginous Eczema. R. Halberstadt.  
Monatschr. f. Kinderh., 1911, x, No. 10.
- Lordotic Albuminuria. (Zur Kenntnis der lordotischen Albuminurie.) F. Hamburger.  
Wien. klin. Wchnschr., Feb. 15, 1912.

- Reaction in Urine of Breast-Fed Infants. (Zur Engel-Turnau'schen Urinreaktion.) D. V. Balazsy.  
Berl. klin. Wehnschr., Feb. 19, 1912.
- Value of Urinary Examination in Infants. F. Van Bogert.  
New York State Jour. Med., February, 1912.
- Vesical Calculus in Boy Aged Five Years. A. D. Smith.  
Am. Jour. Obst., February, 1912.

#### OSSEOUS SYSTEM

- Atypical Case of Acute Epiphysitis in Infant, With Roentgenograms. J. F. Sinclair and H. K. Pancoast, Philadelphia.  
Arch. Pediat., February, 1912.
- A Case of Fragilitas Ossium. W. P. Coues.  
Pediat., February, 1912.
- Bone Transplantation and Osteoplasty in Treatment of Pott's Disease of Spine. F. H. Albee, New York.  
New York Med. Jour., March 9, 1912.
- Defective Bone Growth. (Zur Lehre der Osteogenesis imperfecta.) F. Fuchs.  
Virchow's Arch. f. path. Anat., January, 1912.
- Experimental Rachitis. A. B. Marfan and Feuillie.  
Bull. de la Soc. de pédiat., January, 1912.
- Fracture-Dislocation of the Elbow. W. P. Coues.  
Pediat., February, 1912.
- The Scaphoid Scapula. (Einige Bemerkungen über die Scaphoidskapula und ihre Begeiterscheinungen.) W. W. Graves.  
Wien. klin. Wenschr., Feb. 8, 1912.

#### SKIN AND APPENDAGES

- Annular Livedo in Children. (La livedo annularis chez l'enfant.) Jourdanet.  
Arch. méd. d. enf., February, 1912.
- Treatment of Ringworm of Scalp. J. R. Riddell.  
Glasgow Med. Jour., February, 1912.

#### EYE, EAR, NOSE AND THROAT

- Adenoids in School Children and Their Effect on General System. G. B. Taylor.  
Med. Rec., New York, Feb. 17, 1912.
- Bloodless Enlargement of Nasal Passages. (Die unblutige Erweiterung der Nasenhöhlen.) G. Killian.  
Deutsch. med. Wehnschr., Feb. 1, 1912.
- Infection of the Rhinopharynx. (Les infections rhino-pharyngiennes.) P. Gallois.  
Arch. gen. de méd., January, 1912.
- Membranous Rhinitis: Its Relation to Diphtheria and Its Treatment by Autogenous Vaccine. D. Forbes and H. P. Newshilme.  
Lancet, London, Feb., 3, 1912.
- Menthol in Rhinology and Its Danger for Young Children. (Die lokale Mentholanwendung in der Nase und ihre Gefahr im frühen Kindesalter.) W. Lublinski.  
Berlin. klin. Wehnschr., Feb. 5, 1912.
- Examination for and Treatment of Tonsillitis with Polyarthrititis. (Neues über Untersuchung und Behandlung gewisser mit Polyarthrititis causal verknüpfter Tonsilliten.) P. Roethlisberger.  
München. med. Wehnschr., Feb. 20, 1912.
- Importance of Early Diagnosis of Pathologic Conditions of Adenoids and Tonsils and Treatment. C. J. Whalen, Chicago.  
Chicago Med. Recorder, February, 1912.

- Relation of Age to Tonsillar Infection. H. A. Barnes, Boston.  
Ann. Otol., Rhin. and Laryng., December, 1911.
- Sarcoma of Tonsil. G. Berry, Worcester, Mass.  
Boston Med. and Surg. Jour., March 7, 1912.
- Technic for Operations for Cleft Palate. (Technique de l'urano-staphylorrhaphie.)  
L. Ombrédanne.  
Jour. d. Chir., January, 1912.

## THERAPEUTICS

- Benzin Poisoning of Infant. (Eine akute Benzinvergiftung beim Säugling.) A. Friediger.  
München. med. Wchnschr., Jan. 30, 1912.
- Cod Liver Oil. (Beitrag zur Lebertrantherapie.) A. Czerny.  
Therap. der Gegenwart, February, 1912.
- Dangers of Menthol. (Dangers et méfaits du menthol.) R. Leroux.  
Presse méd., Feb. 7, 1912.
- Diuretic Action of Digitalin and Theobromin in Children. (Etude de l'action diurétique de la digitaline et de la théobromine chez l'enfant.) P. Nobécourt and G. Paiseau.  
Arch. méd. d. enf., February, 1912.
- Necrosis of the Jaws from Mercurial Salve Applied to Burn. H. L. Rocher.  
Jour. de méd. de Bordeaux, Feb. 11, 1912.
- Vaccine Therapy in Children. J. W. White.  
Virginia Med. Semi-Month., Feb. 9, 1912.

## SURGERY

- A Case of Repair of Facial Defect. Raymond C. Turek.  
Jour. Am. Med. Assn., Feb. 17, 1912, p. 469.
- Surgical Conditions of Childhood. J. T. Buston.  
Virginia Med. Semi-Month., Feb. 9, 1912.

## MISCELLANEOUS

- The Child That Is to Be. C. B. Reed, Chicago.  
Chicago Med. Recorder, February, 1912.
- The Food and Medicinal Value of Wine. W. E. Fitch.  
Pediat., February, 1912.
- Children's Untruths. (Sobre a mentira infantil.) P. Olinto.  
Brazil Medico, Jan. 15, 1912.



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## THE TONSILS IN CHILDHOOD \*

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The tonsils have attracted many investigators, but the results of the investigations are unsatisfactory and often contradictory. Connected by many in a very direct way with local disease elsewhere as well as with systemic disturbances, it is especially necessary because of the incompleteness of our knowledge that we should have our attention directed at times to their functional side lest we rashly assume that the tonsils are to be regarded as a constant menace to health. It will therefore not be out of place to restrict my remarks chiefly to the relation of their function, so far as we at present know it, to disease, and along these lines to indicate the general principles that should underlie our treatment, rather than to specify the particular treatment adapted to any special variety of disease which they present.

We may regard disease as a condition of disturbed or imperfect function or of the results of disturbed function. The day is past when pathology was a study of morbid anatomy; it is now to a large extent a study of morbid physiology. Therefore, to observe correctly and record accurately the signs and symptoms of the disease of any organ, we must necessarily have a clear picture of its physiologic function. Failing to get such a picture, we must fall back on such anatomic facts as bear on the function. Since disease, though local in its outward manifestations, is systemic in its effects, we again require to fall back on anatomy and physiology so as to correlate correctly the disturbance of function with pathologic and bacteriologic changes produced elsewhere. Only thus can we hope to gain an intelligent grasp of ultimate conditions.

So it appears to me that in approaching the subject of the tonsil, shrouded as it is with so much uncertainty, it would be well to emphasize such points in its anatomy and physiology as appear important for the clinician to have recalled, and especially as some of these are too often overlooked or misinterpreted. Many of our errors in local treatment have resulted from failure to grasp some fundamental fact in its anatomy or physiology. Some of our failures can be traced to an inability to correlate intelligently the relation of systemic results to local causes or local results

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\* Read before the Chicago Pediatric Society, Feb. 20, 1912.

to systemic causes. It will be especially necessary for me to emphasize these anatomic and physiologic observations, since I shall present to you some conclusions which I have been forced to draw from them, bearing on tonsillar disease especially relevant to the pediatrician. Further, I shall dwell on these observations since I believe the clearing up of many of the enigmas associated with the pharyngeal tract necessitates not only a clear conception of the present state of our knowledge, but a cooperation of pediatrician with laryngologist.

The ease with which the palatine tonsil is observed and the association which it has in the minds of many with all kinds of diseases, lead often to a self-satisfying yet inaccurate diagnosis. Forgetful of its intimate relation to pathologic processes in the nose and nasopharynx, and of its frequent association with systemic disturbances, we too readily diagnose as a primary pathologic condition what is in reality a secondary pathologic result. In a tonsillar enlargement we often erroneously see an active pathologic process instead of a hyperfunctionating organ.

My remarks apply particularly to the palatine tonsils, usually referred to as "the tonsils," and to the pharyngeal tonsil lying in the nasopharynx, enlargements of which we loosely speak of as adenoids. Anatomically we possess a fairly clear picture of their structure and a fairly accurate knowledge of their phylogenetic and ontogenetic history, especially of the palatine tonsils. Physiologically so much is even yet obscure that in the minds of many this lack of knowledge is taken to mean that we must regard the tonsil as of no importance. To this some have added a baneful association with all kinds of diseases, and so they reach that ultranegative stage in which the tonsil becomes an actual menace to health. Gradually, however, evidence is accumulating which is helping to a clearer understanding.

On the *anatomic* side the facts I wish briefly to emphasize are:

1. The palatine tonsil is present in all mammals, with one or two noteworthy exceptions in rodents. Thus the rat and guinea-pig have no tonsils. I can confirm the opinion of other investigators in regard to the rat, that not only are no tonsils present, but there is no sign in the embryo of any tonsillar anlage. The significance of their absence has so far not been explained. From a comparative study it would appear that the size of the tonsil bears no relation to the species, but apparently has relation to the size of the animal.<sup>1</sup> The anatomic location of the tonsil is such that no matter how it be concealed by folds of mucous membrane, it always retains a communication with the pharynx. I have been much impressed with this fact from observations made in my laboratory during the past winter, especially in carnivora. In this genus the tonsil is often so protected by folds as to be invisible from the mouth, no doubt influ-

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1. Poole, C.: Thesis for M.A. degree, Northwestern University, 1911.



enced by the character of the food devoured. But there always exists a channel of communication with the pharynx. This is well seen in the lion, in which the tonsil lies in an elliptical sac of considerable size in the lateral pharyngeal wall, occupying but a portion of one side. The sac communicates with the pharynx by a relatively small opening, and is so placed that during certain movements of the pharynx the contents can be expelled into the back of the mouth. Therefore, comparative anatomy suggests in the varied relations which the tonsil bears to the pharynx, the necessity of a direct communication between the tonsil and pharynx along which secretion or excretion may pass from the tonsil to the pharynx.

2. In all mammals the tonsil does not develop like a lymph-node from a plexus of preexisting lymph-vessels in the mesothelium. It develops as an ingrowth of endothelium from the second branchial pouch, and later lymphoid tissue appears in the mesothelium around these ingrowing buds. In origin it comes into line with the thymus and the thyroid. Therefore developmentally the tonsil is not a lymph-node.

3. When we examine the life history of the tonsil we find that it appears early in embryonic life (fourth month), reaches maturity at the end of the first year of infancy, and at or about puberty tends to diminish in size. In the adult the reticular tissue and follicles are more or less atrophied. From these facts we may say that there is good ground for the belief that the physiologic activity of the tonsil is of greatest importance in early life.

On the *physiologic* side our knowledge of the tonsil is extremely meager. We know that in its deeper tissue we have lymph-nodules, some with germ centers showing the proliferation of lymphocytes which pass either internally into the lymphatics or externally into the crypts of the pharynx, constituting part at least of the so-called salivary corpuscles. As Stohr<sup>2</sup> pointed out, the exudation of leukocytes is physiologic and not inflammatory, since it is observed in healthy children and at the end of embryonic life. In healthy individuals the exuded leukocytes do not succumb at once, but mix with the alkaline mouth secretions, and according to Grober,<sup>3</sup> on a warm stage show ameboid movements. But what is their further action? Do they act as phagocytes or do they give up enzymes? Metchnikoff<sup>4</sup> has no doubt about the answer:

The tonsils and other lymphoid organs are traversed by an enormous number of leukocytes which execute a kind of migration toward the cavities containing microorganisms. It is evident that we have here a process of phagocytic defense. When we remove a particle of mucus from the surface of the tonsils of a person

2. Stohr: Zur Physiologie der Tonsillen, Virchows Arch. f. path. Anat., 1884, xcvi, 211; Biol. Centralbl., 1882.

3. Grober: Tonsillen als Eintrittspforten für Krankheitserreger, Klin. Jahrb., 1905, xiv, Part 6.

4. Metchnikoff: Immunity in Infective Diseases, 1905, Cambridge Univ. Press, p. 415 and 428.

in good health we always find that it contains leukocytes, especially microphages, filled with microorganisms of all kinds.

In further explanation of the defensive properties he continues:

The buccal cavity has a very rich microbial flora. It is astonishing that in spite of this state of things, wounds in the mouth heal very rapidly, and operations on the buccal cavity done with insufficient or no aseptic precaution do not, in the great majority of cases, set up infective complications of the slightest importance. It is often asked how under these conditions does the mouth defend itself against the vast number of formidable microorganisms? Powerless as an antiseptic, the saliva fulfils an important function in ridding the mouth of microorganisms in a mechanical way, cleansing and washing them away, mechanically to the exterior, more frequently into the stomach. In addition to the direct mechanical part played by the saliva, it performs a very important indirect function. This fluid contains microbial products and diastases, and is capable of exciting in the leukocytes a positive chemiotactic activity. The influence of the saliva on the afflux of the leukocytes must be regarded as an act important for the protection of the buccal cavity, and it is probably due to this attraction of leukocytes that lesions of this region heal so quickly. The leukocytes are very numerous in the glands of the mouth and the tonsils always supply large quantities of them.

Before leaving this phase of the subject I would add that from observations recently made at the Wesley Hospital I have been led to believe that in systemic diseases we may have this exudate very considerably modified, and according to Grober<sup>5</sup> it may disappear during diseases which accumulate leukocytes within the body.

But from the activity of the tonsil in fetal life, as shown by the fact that at birth the crypts and tonsil lymph-sinuses are found to contain lymphocytes, it would appear that the exudation from the tonsil cannot have only a relation to bacterial invasion of the pharynx. Its greatest activity being during developmental life, would suggest some additional function. From our knowledge of leukocytes, and with the experiments of Kroeppe<sup>6</sup> in mind, I cannot but feel that we have in the tonsil an organ combating some constituent of metabolism which may appear in the lymph-channels or in the nasopharynx, a constituent which if passed into the blood-stream would be hurtful to the individual. When this product of metabolism is arrested or disappears the leukocyte activity ceases and the gland is converted into ordinary connective tissue, the germ center to be the last to go. It has been suggested that tonsillar metabolic processes are connected with development of the teeth.<sup>6</sup> This may be so; but let us not forget that there are other complex processes going on in the upper respiratory and alimentary tracts in childhood. Under the circumstances it would be well to wait for further observations.

From the above anatomic and physiologic data I have drawn the following *conclusions*:

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5. Kroeppe: See Gulland, Development of Lymphatic Glands, Jour. of Path. and Bact., 1894, p. 476.

6. Wright: Boston Med. and Surg. Jour., May 20, 1909.

1. Since comparative anatomy shows that in all cases a communication with the pharynx has been preserved, it would appear that intimate relationship with the pharynx is a necessity of tonsillar activity.

2. The tonsillar activity is to be regarded as most active during developmental life. There is no evidence that in man it should be regarded as a recessive organ.<sup>7</sup>

3. The tonsil cannot be regarded as merely a lymphatic node. Though it presents microscopically adenoid tissue, yet its developmental history and its physiologic activity at least make us pause before drawing such a conclusion. It is just this presumption that has led many to a hasty and unnecessary enucleation. The statement some have made that since the tonsil is only a lymphatic gland its activity can be readily replaced by other lymphatic structures is of very doubtful merit even so far as lymph-nodes are concerned, and erroneous so far as the tonsil in the child is concerned.

4. We have every reason to believe that the tonsil plays an important rôle in the complex changes which occur at the upper end of the alimentary tract. The argument that no one has seen any local or systemic deficiency following removal of tonsils in childhood does not satisfy me, since we have not sufficient observations based on complete enucleations. Complete enucleation is at all times difficult, as one can see on examining the deeper anatomic appearance of an enlarged tonsil.<sup>7</sup> Further, we cannot know what damage may be done till we have a clearer conception of its function. Let the pediatrician watch judiciously cases of tonsil removal and from him and not from the laryngologist I will expect to hear before long of some observation which may be more than a mere coincidence between tonsillar enucleation and systemic effects. Already we have a few suggested.

As an outcome of these anatomic and physiologic considerations I have been led to believe that in the child we are dealing with an organ which functionally differs considerably from the same organ in the adult. I therefore distinguish in the life-history of the tonsil *two distinct periods*:

(a) Before puberty — period of functional activity.

(b) After puberty — when it persists chiefly as an aggregate of lymph-nodules which tend to atrophy.

This point of view very considerably modifies my views in regard to tonsillar diseases and their treatment. In the child it should be conservative, so far as possible, and the younger the child the more conservative; in adults let it be radical whenever necessary.

What is a normal tonsil in childhood?

When we turn to anatomic authorities for assistance in answering this question we are met with great difference of opinion. Few consider the

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7. Wilson, J. G.: Some Anatomic and Physiologic Considerations of the Fauical Tonsil. Jour. Am. Med. Assn., May 26, 1906.

question of size in the child as distinct from the adult, and so the figures are very divergent. As a fairly reliable basis I may quote from Cunningham<sup>8</sup> in regard to the size of the normal tonsil in early life: length, 20-22 mm. (1 inch); breadth, 18-20 mm. (three-fourths inch); thickness, 12-15 mm. (one-half inch). These, I presume, are post-mortem figures, though he does not say so.

Leaving the anatomist and coming to the laryngologist, the best figures I know of are given by Gleason<sup>9</sup> with regard to a child of 6: length, 1¼ inches; breadth, three-fifths to 1 inch; thickness, three-fifths to 1 inch. Again I do not know how he arrived at these figures, though it is evident from his remarks that he regards the tonsil as reaching its maximum size about that age.

Without desiring to discuss the relative value of these figures I should like to point out the following:

1. It is impossible to estimate the thickness of the tonsil at any post-mortem, especially after a chronic illness. These bodies shrink very considerably during the last stages of disease, as well as after death, as a result of their great vascularity.

2. The most reliable data have been got when the tonsil has been removed immediately after sudden death.

I am not aware of sufficient figures derived during life from young healthy children which would establish a normal. My observations would agree more with those of Gleason than with those of Cunningham, though if Cunningham's observations were post mortem and Gleason's observations were made during life or immediately after death in a brief illness, the discrepancies are not so marked. I believe that in a child the healthy tonsil projects beyond the anterior pillar of the fauces; that at the age of 6 to 12 it is not normal to find it concealed behind the pillar. Considerable variation in this projection is consistent with health, not only at different periods in childhood, but even in a child. I do not believe that we can assign to a body so vascular and so responsive in childhood a definite depth or projection beyond the pillars below or beyond which it is abnormal.

We pass now from the résumé of anatomic and physiologic data to an application of our deduction from these data to some varieties of tonsillar disease. All are agreed that if the tonsil be diseased it should be removed. To this I would add that if so responsive a body appears functionally inactive and a probable source of disease its treatment or removal ought to be considered. But it is sometimes not so simple a matter to recognize a tonsil which demands removal because of disease. It is not so easy to say whether it is diseased primarily or whether its pathologic appearance

8. Cunningham, O. T.: *Text-Book of Anatomy*, New York, 1909, p. 1036.

9. Gleason, E. B.: *Diseases of Nose, Throat and Ear*, Philadelphia, 1910, p. 181.

may not be secondary to disease elsewhere, either in its immediate neighborhood or arising from systemic causes. In children it may be necessary to consider whether there is here a *hyperfunctionating* or *hypofunctionating* organ. Many large tonsils have been found to differ little if at all from a normal tonsil. Many tonsils macroscopically small and innocent looking have been found microscopically to contain numerous foci of infection.

Very little attention has been paid to the small palatine tonsils in children. As an outcome of my anatomic and physiologic beliefs, and as a result of observations in the clinic, I feel that we ought to consider these more carefully than we do at present. In the present status of medical practice they come more usually under the observation of the pediatrician than of the laryngologist, for such has been the trend of our teaching that in children we consider only such to be locally diseased as are enlarged or show signs of recurring inflammation. Such tonsils appear in children as small pale structures often concealed behind the pillars of the fauces, flabby in consistence and with wide mouthed crypts, often with whitish looking epithelium at their entrance. Microscopically I have frequently noted hyaline degeneration and minute foci of inflammation within the tissue. Sometimes half the tonsil is atrophied and the other half shows a ragged granulating pharyngeal surface projecting beyond the pillars. These hypofunctionating bodies may be associated with general pharyngeal attacks of a more or less acute nature in which the tonsil appears to play a subordinate rôle. They are apt to be associated with glandular enlargement in the cervical region. But it is when we regard the tonsil less in its local than in its systemic potentialities that we will have our attention fixed more and more on the atrophic variety. In a child when considering the tonsil in its causal relation to systemic disease I should regard with much more suspicion a small tonsil than a tonsil remarkable for nothing but its size. I have removed in a child of 8 such a tonsil associated with mild pharyngeal attacks, for persistent slight temperature associated with recurring rheumatic attacks, and with satisfactory results.

The enlarged tonsil so frequent in early life may show great variation in size consistent with a healthy organ. A large tonsil in a child is not necessarily pathologic; a normal tonsil may project considerably beyond the pillars. In many systemic diseases, apart from any local affections, it becomes enlarged. Mere fluctuation in size in a child ought not to be regarded as a sign of disease and an indication for enucleation. Many children are constitutionally subject to such fluctuations and the treatment is general more than local. It is common knowledge that in systemic diseases we have such enlargements and few of us are now disposed to argue that this enlargement is a sign of focal disease. I would rather regard it as an indication of functional activity. We cannot judge of

the condition of a tonsil from its appearance during an acute attack, for not only in systemic disease but in disease elsewhere in the nasopharynx the tonsil may become secondarily affected and may be only manifesting a hyperfunctionating activity. It is so easy to look into a throat and find an inflamed area with enlarged tonsils and arrive at a too hasty conclusion in regard to the cause of the illness.

In children many of the symptoms attributed to enlarged tonsils, such as anemia, buccal respiration, snoring, suffocative symptoms, inframammary depression of the ribs, ill-developed thorax, and especially eustachian deafness, are usually due to concomitant adenoids. But there are certain well-defined symptoms which indicate when we may well interfere. In this respect I cannot do better than give the following excellent summation from two well-known laryngologists:<sup>10</sup>

Chronic enlargement of the tonsils may then act injuriously in three different ways, namely, (a) by mechanically obstructing the food and air passages; (b) by maintaining a liability to frequent, often very painful attacks of inflammation within the glands themselves or in their immediate neighborhood, and by the chronic toxemia from the contamination of the blood circulating through the tonsil, causing the so-called "poor circulation" or lack of normally active tissue-metabolism so often seen in patients with enlarged tonsils; (c) by forming a perpetual source of danger from infection by various microorganisms, such as those of diphtheria or tuberculosis (page 169).

I have quoted this paragraph *in extenso*, though as my previous remarks indicated, I would make some reservation in regard to the last sentence. In enlarged glands I have never found tubercle primarily present; this, however, I will discuss later. It is, however, a daily experience that such tonsils are subject to repeated attacks of inflammation and so may be legitimately removed.

In discussing the relation of focal disease in the tonsil to disease manifesting itself elsewhere, it may be asserted that there is sufficient evidence to lead us to conclude that some such relationship exists. This is what we would expect when we reflect that no disease is absolutely local and many react deleteriously on a distant part which is physically weakened from some cause, constitutional or otherwise.

To narrow our remarks down to specific example we may refer to the relation of tonsillar disease to arthritis or endocarditis. As I have said elsewhere,<sup>11</sup> there is sufficient clinical evidence to lead us to believe that a focus of infection anywhere in connection with serous or mucous surfaces may result in arthritic or cardiac affections, and that the removal of such a focus is often followed by the amelioration of such affections. Investigation has demonstrated that streptococci derived from various sources may produce arthritis and endocarditis in rabbits. Further, it would appear that the channel of introduction is of minor importance.

10. Semon and Watson: *System of Medicine*, Allbutt and Rolleston, London, 1908, p. 169.

11. Wilson, J. G.: *Illinois Med. Jour.*, February, 1912, p. 221.

At present the evidence seems to be to suggest the association of various organisms with this relationship rather than a special microbe, but on this point I would refer to the recent work of D. J. Davis,<sup>12</sup> who has justly qualified himself to speak with authority.

It is to be expected that we should find such examples to abound in connection with chronic focal infections in the nose, mouth and pharynx, where various strains of streptococci are found in abundance. It must be admitted that a chronic focal infection in the tonsil may bear some causal relation to arthritic and cardiac affections. But the frequency of the focal infection and the infrequency of a concomitant or subsequent arthritic affection speak against the relative importance of such a seat and suggest that some other factor has to be taken into account. My present attitude in regard to the etiologic relation of the tonsil to endocarditis and articular rheumatism may be summed up in this, that if the tonsil be subject to recurring attacks of inflammation it is not alone the tonsil which is vulnerable. It makes all the tissue in the nasopharynx more susceptible to infection. We thus have a large area from its position exposed to microbial attacks. Thence comes the initial factor in the chain which may lead through unknown paths to distant pathologic processes.

Primary tuberculous disease of the tonsil is rare; disease foci secondary to pulmonary disease is not uncommon, the general belief being that there has been infection from the sputum. It is interesting here to note that it is not the enlarged hyperfunctionating gland that usually becomes primarily tuberculous, but the small hypofunctionating organ. Many observers have found tubercle bacilli in the tonsil, apart from actual disease, but the finding of this bacillus in the tonsil is not to be wondered at and is not indicative of disease, for they may get there through its lymphatics which connect with the nasopharyngeal mucosa, as well as by in-wandering from the pharynx. When we consider the liability of the child to tuberculous invasion, and the anatomic structure and position of the tonsil exposing it to infection in a way that few other organs are exposed, then add to this the continual rupture of its pharyngeal walls from exudation of leukocytes, the wonder is not that tubercle bacilli are to be found, but that primary tuberculous tonsils are rare. If the soil were as favorable as the bacteria are common, tuberculous tonsils would be the rule, not the exception. In children the invasion from the nasopharynx of the cervical lymph-nodes is undoubted, but tuberculous disease is but one of many causes of enlarged nodes, and the tonsil is but one of many sources. When the tonsil is at fault, I believe it is more often the small hypofunctionating tonsil which is to be found. It is an everyday experience that enlarged cervical lymph-nodes are often associated with tonsillar disease and that removal of this focus of disease frequently

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12. Davis, D. J.: Jour. Am. Med. Assn., July 2, 1910, p. 26.

causes the glands to reduce in size. But in a majority of cases in children to make the diagnosis that these glands are tuberculous secondarily to enlarged tonsils rests on insufficient ground. The infrequency of primary tonsillar tuberculous disease, the rapid growth of these glands, and their rapid disappearance after removal of the tonsils appear to me to speak against their tuberculous nature. Another frequently expressed statement is that there is a special and direct connection between the tonsil and the apex of the lung for tuberculous invasion. This appears to me to be disproved on anatomic grounds, for no such direct connection between the cervical lymphatics and pulmonary lymphatics at the apex exists.

Before enlarged chains of nodes are removed from the neck it should be regarded as imperative that the nose, nasopharynx and pharynx be carefully examined to ascertain a possible source from which these nodes have become infected. Sometimes as a result of such an examination the complete surgical removal of cervical lymph-nodes now objected to on general principles would become unnecessary.

In conclusion let me say that my endeavor has been, so far as our knowledge at present permits, briefly to point out the probable function of the tonsil to metabolic processes and to diseases in the upper respiratory and alimentary tracts, but especially at their junction in the pharynx. As knowledge advances there is constantly impressed on us the important and unexpected relation of this region to disease. For instance, let me refer to its relation to cerebrospinal meningitis and poliomyelitis. We shall err if we forget that the essential resisting power of this tract to infection lies in its tissue cells. Further, we shall add to this error if we concentrate our attention too much on leukocyte invasion or exudation to explain initial protection. Whenever from unhygienic surroundings or mode of life, it may be also from constitutional weakness, the tracts are exposed to influences which lower their vitality, the tonsils suffer for them and with them. When the mucous surfaces, particularly absorbent in the child, are exposed to irritation, the tonsil again suffers for and with them. To me the tonsil in a child protects these tracts, especially where the two come together in the nasopharynx, and is associated directly with their well-being. If this be so, I am called on to do everything to protect these bodies during the period of functional activity. Further, I am called on to remove them when I am convinced that on account of disease or loss of function they are not only a source of infection but are having an injurious effect on the structures around.

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## A COMPARISON OF THE STREPTOCOCCI FROM MILK AND FROM THE HUMAN THROAT

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The present comparative study of throat and milk streptococci was undertaken with the object of establishing a method for distinguishing between organisms isolated from these two sources. Much confusion has existed as to the relationships within this genus. The introduction of the biometric study of the streptococci according to their reaction in various carbohydrate mediums by Gordon (1904-1905) and the subsequent extension of the study by Houston (1905-1906) seemed to give a method of solving this obscure problem. The English results have been obtained by the use of litmus added to the mediums and the reactions recorded as positive or negative according to the color of the litmus, without titration. If the mediums were not neutral at the start, it is obvious that they must have classified many organisms as fermentors which have only very slight fermentative properties and really belong to the non-fermenting group. Winslow has pointed out that "they include a much greater percentage of positive records than the American ones."

TABLE 1.—PERCENTAGE OF CULTURES GIVING MORE THAN 1.1 PER CENT.  
ACID AT 37 C.

Fermented. .....	Per cent. Throat Cultures.	Per cent. Milk Cultures.
Dextrose only .....	22.2	6.3
Dextrose and lactose.....	20.4	38.0
Dextrose, lactose and saccharose	33.1	57.7

TABLE 2.—PERCENTAGE OF CULTURES GIVING MORE THAN 0.5 PER CENT.  
ACID AT 20 C.

Fermented. .....	Per cent. Throat Cultures.	Per cent. Milk Cultures.
No fermentation .....	50.0	0
Dextrose only .....	40.0	32.5
Dextrose and lactose.....	1.8	31.0
Dextrose, lactose and saccharose	0	31.0

Winslow introduced the method of titrating the cultures with phenolphthalein as an indicator, and at present this procedure seems to give a substantial basis for fixing the relationships within this group.

We examined seventy pure strains of streptococci isolated from fresh specimens in our laboratory. Cultures taken from sore, inflamed, or

otherwise unusual throats have been grouped as "abnormal." The small number of cultures used renders our generalizations more or less tentative, and it is our intention to substantiate the work, using larger numbers. Quantitative acid production was studied in six carbohydrate mediums: dextrose, maltose, lactose, saccharose, raffinose and mannite. Two tubes of a 1 per cent. carbohydrate broth were inoculated<sup>1</sup> at the same time, one tube being placed at 20 C. and the other at 37 C. for seventy-two hours. Five c.c. were then drawn off with a pipet, diluted with 45 c.c. of distilled water and titrated against twentieth normal sodium hydroxid, using phenolphthalein as an indicator. Blank tubes were incubated with the

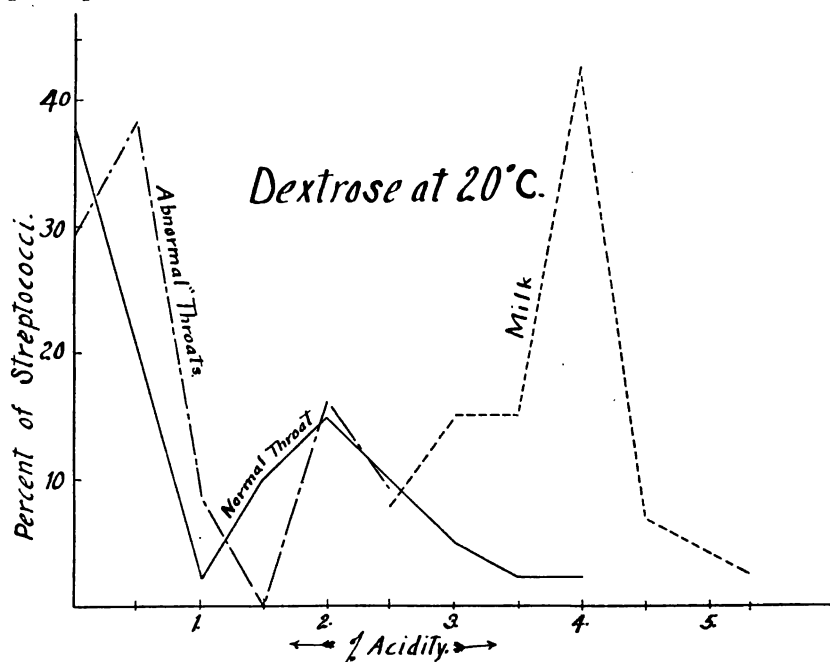


Chart 1.—Showing percentage of acidity and streptococci from abnormal throats, normal throats and milk cultured in dextrose at 20 C.

inoculated tubes and these were titrated at the same time. The difference between the blanks and the cultures was recorded as the amount of acid produced. We have omitted the maltose results in classifications tables, as the figures follow the lactose figures fairly closely. With the sugars that are fermented at all at 37 C., the first reaction mode was found to fall at or beyond 1.2 per cent. acidity expressed as normal acid, and we have used this as the dividing point between a positive and a negative reaction.

1. The inoculations were made by transferring two standard loops full of the growth found in the water of condensation on North's gelatin agar medium.

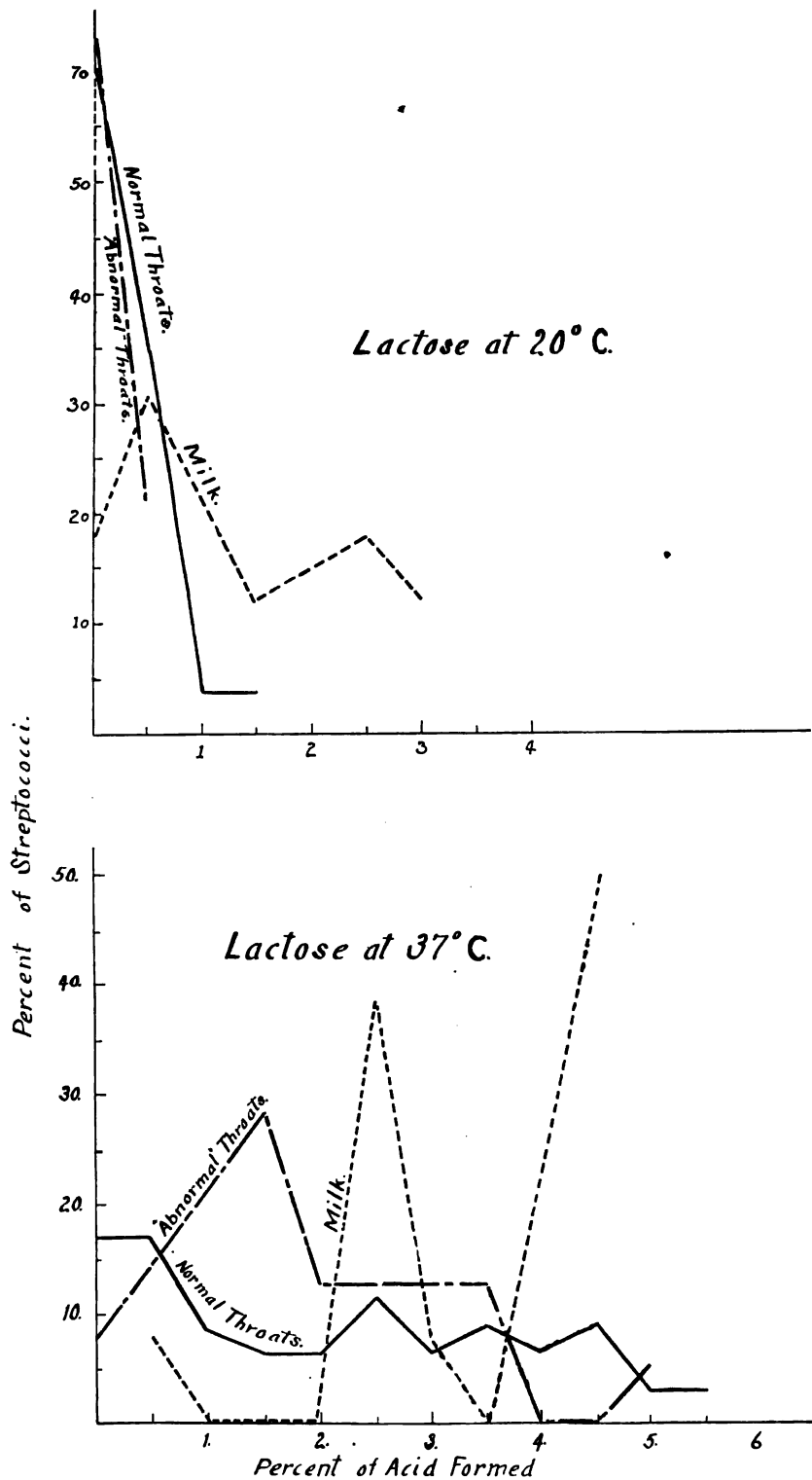


Chart 2.—Showing percentage of streptococci and acidity from normal and abnormal throats and milk cultured in lactose at 20 and 37 C.

On this basis, all but four cultures fermented one or more of the mediums used. It was found that 83 per cent. of these might be placed in three groups according to their fermenting capacity.

When incubated at 20 C. the first reaction mode falls at 0.5 per cent. acidity and on this basis the milk cultures fall into the same general groups as noted above, but the throat streptococci show 50 per cent. not fermenting at all, and 40 per cent. fermenting dextrose only.

It will be noted that the carbohydrates were attacked progressively in the order of the complexity of the molecular structure, the single sugar

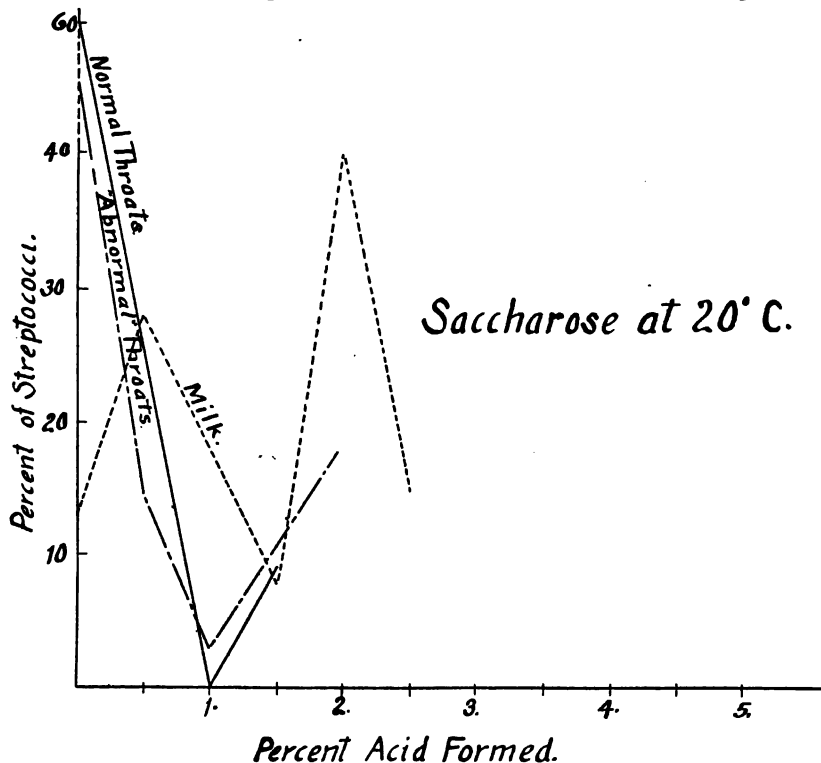


Chart 3.—Showing percentage of acidity and streptococci from normal and abnormal throats and milk cultured in saccharose at 20 C.

being most easily fermented, then the disaccharids, the trisaccharid and the alcohol being too complex to be used except by a very few cultures. It is seldom that a strain reacts with a sugar lower in the scale of fermentability while failing to attack all the simpler, more available ones, as is shown from a study of the tables at the end of this paper. Andrews and Horder suggested this grade of availability in 1906, referring to the phenomenon as "a set of gymnastic exercises in chemical decomposition." The colon group shows a similar metabolic relationship toward the carbohydrates but with them the size rather than the structure of the molecule

seems to be the controlling factor. Howe (1911) has aptly called this order of availability the "metabolic gradient." It suggests a very important advance in the biometric method.

A consideration of the reactions in the individual sugars brings out the following facts:

*Dextrose*: The normal throat strains seem to show the greatest fermentative properties, their mode coming at 6.0 per cent. acid when grown at 37 C. The milk cultures show a very specific reaction, all falling into a group giving from 3.5 per cent. to 5.5 per cent. acid. Reference to

TABLE 3.—STREPTOCOCCI ISOLATED FROM NORMAL THROATS

Sample No.	Long or Short Chain Form	Reaction	Percentage of Acid Formed in—											
			Dextrose.		Lactose.		Maltose.		Saccharose.		Raffinose.		Mannite.	
			37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.
1	Short	G +	7.3	3.5	.3	0	..	..	3.0	.1	1.1	0	0	0
2	Long	G +	3.3	1.9	3.7	0	.9	0	1.8	.1	.2	.1	.1	0
3	Long	G +	3.8	2.4	4.6	.3	1.6	.1	2.6	0	—1	—1	0	0
4	Short	G +	6.1	1.8	6.1	.2	2.7	.2	2.1	0	.3	0	0	.2
5	Short	G +	6.5	1.3	2.0	.2	.9	0	1.6	0	0	0	0	0
6	Short	G +	5.0	2.1	5.4	0	1.7	0	.1	1.4	.1	0	.2	.1
7	Short	G +	3.6	1.1	4.1	0	.6	.1	.8	0	.3	0	0	0
8	Long	G +	4.3	1.7	—1	—	1.5	1.1	1.1	1.3	1.3	0	.2	.2
9	Short	G +	5.7	1.7	—5	0	..	..	1.9	.1	1.1	0	0	0
15	Short	G +	4.2	2.6	0	.2	1.6	.4	.1	0	—1	.2	.1	0
16	Short	G +	.8	.9	.3	.6	..	..	0	.2	—3	0	0	0
17	Short	G +	4.2	2.2	4.3	0	..	..	0	0	1.7	0	.1	0
18	Long	G +	3.1	1.8	3.7	0	0	0	0	0	0	0	0	0
19	Long	G +	2.7	1.2	3.4	.5	0	0	0	0	—1	0	0	0
20	Short	G +	4.5	3.8	..	..	..	..	..	..	1.4	..	..	..
21	Short	G +	6.0	3.4	..	..	..	..	..	..	1.2	0	..	..
22	Short	G +	5.9	3.0	.1	.1	.9	.1	0	0	.1	0	0	0
24	Short	G +	6.0	.5	..	..	..	..	.8	.5	.2	0	..	..
25	Short	G +	6.0	1.6	4.1	0	2.9	.2	—1	0	1.0	0	.1	0
26	Short	G +	6.2	1.4	2.2	0	2.9	.3	0	.2	.1	0	0	0
27	Short	G +	6.3	.3	2.5	0	2.5	.1	2.1	0	.1	0	0	0
28	Short	G +	6.0	.2	3.0	0	2.8	0	1.4	0	—1	.1	.1	0
29	Short	G +	5.8	2.4	0	0	..	..	3.2	0	.9	.1	0	0
32	Short	G +	4.5	0	1.5	0	1.4	0	1.5	.8	1.1	0	0	0
33	Short	G +	5.1	0	.5	0	.5	.2	.9	0	.1	.3	0	0
34	Short	G +	2.0	.1	.2	0	.5	0	0	0	.4	0	0	0
35	Short	G +	4.8	.3	2.5	2.2	2.5	2.2	3.5	.1	.2	.1	0	0
36	Short	G +	3.8	.2	.6	.2	.6	0	.1	0	.2	.1	.2	0
38	Long	G +	4.0	.0	1.7	0	1.3	.2	1.1	1.1	0	.1	0	0
43	Short	G +	3.8	.1	3.3	0	0	0	1.5	0	0	0	0	0
44	Short	G +	1.5	0	3.1	0	2.9	0	2.0	.2	.1	0	0	0
45	Short	G +	5.4	0	0	0	..	..	.9	0	0	0	0	0
46	Short	G +	..	..	..	..	..	..	..	..	..	..	0	0
47	Short	G +	5.8	0	2.4	0	2.3	.2	2.6	0	.4	0	0	0
48	Long	G +	0	0	.6	.1	.7	.3	0	0	.8	0	0	0
49	Short	G +	4.6	.5	1.2	0	1.5	0	2.4	0	1.1	0	0	0
50	Short	G +	6.0	0	2.6	0	2.5	.2	1.9	0	.1	0	0	0
51	Long	G +	5.4	0	0	0	1.2	0	.2	.1	0	0	0	0
52	Long	G +	3.8	—3	1.6	.1	1.5	0	1.1	.1	.2	0	0	.1
53	Long	G +	3.5	0	0	0	2.1	0	.4	0	.6	0	0	0
54	Short	G +	1.1	0	.1	0	.4	0	.8	0	.1	0	0	0
55	Long	G +	1.7	0	.7	0	0	0	.4	0	.1	0	0	0

Chart 1 shows the 20 degree results plotted. Only about 10 per cent. of the throat strains give over 2.5 per cent. acid, while all of the milk cultures give a higher percentage than this.

*Lactose:* We find here a fairly even distribution of the throat strains at 37 C., while the milk streptococci all give high acidity. At 20 C. lactose proves much more available for the milk than for the throat cultures, as is clearly shown in Chart 2.

TABLE 4.—STREPTOCOCCI ISOLATED FROM "ABNORMAL" THROATS

Sample No.	Long or Short Chain Form	Reaction	Percentage of Acid Formed in											
			Dextrose.		Lactose.		Maltose.		Saccharose.		Raffinose.		Mannite.	
			37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.
68	Long	G +	5.5	1.2	0	0	1.8	.4	1.9	1.3	1.4	0	0	0
69	Long	G +	6.2	0	4.7	0	..	..	2.1	1.7	.2	0	0	0
30	Short	G +	5.2	2.2	.3	.3	2.0	1.4	2.0	1.8	.1	.2	.1	0
31	Long	G +	2.3	.6	.1	0.0	..	..	0	.1	0	0	0	0
37	Short	G +	4.3	1.7	..	..	..	..	..	..	0	.1	0	0
57	Long	G —	3.3	1.9	2.7	2.4	1.7	.8	0	0	.2	0	.3	0
58	Long	G ±	1.5	.1	1.4	.1	1.8	.8	.9	.1	.4	.1	.2	0
59	Long	G ±	1.5	.3	1.5	0	.8	0	2.0	0	.3	0	.2	0
60	Short	G +	3.1	0	2.9	0	2.8	0	2.8	0	0	0	.1	0
61	Short	G ±	1.8	.1	1.8	0	1.9	.2	1.7	0	1.5	0	0	0
62	Short	G +	3.2	0	3.5	0	2.8	0	3.1	0	0	0	0	0
63	Long	G +	1.6	.1	1.6	.1	1.7	0	1.0	0	.3	0	0	0
64	Short	G +	1.9	.3	1.9	0	2.1	.9	.2	0	1.7	.1	.2	0
65	Short	G +	3.4	0	3.2	0	2.8	.8	0	0	1.5	0	0	0
66	Long	G +	..	..	1.5	0	1.7	0	.1	0	.3	0	.1	0

TABLE 5.—STREPTOCOCCI ISOLATED FROM MILK

Sample No.	Long or Short Chain Form	Reaction	Percentage of Acid Formed in											
			Dextrose.		Lactose.		Maltose.		Saccharose.		Raffinose.		Mannite.	
			37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.	37 C.	20 C.
10	Long	G +	4.1	3.4	4.0	0	1.6	0.2	2.0	1.1	1.6	0	.4	0
11	Long	G +	4.1	4.0	.4	0	2.0	1.0	1.0	.4	.2	0	0	0
12	Long	G +	4.4	3.9	4.1	1.5	2.3	1.1	2.3	2.1	.1	0	.1	0
13	Long	G +	3.2	3.9	4.2	4.2	1.3	.5	2.1	2.1	0	.2	.1	0
14	Long	G +	4.3	3.8	4.5	.3	2.1	1.1	1.8	2.0	0	.2	.1	0
23	Long	G +	4.0	5.8	2.2	2.4	1.9	1.9	0	0	— .1	0	0	0
39	Long	G +	5.4	4.8	2.6	2.6	1.6	1.9	0	0	0	.1	0	0
40	Long	G ±	5.2	4.1	2.5	2.5	1.7	1.4	.1	.1	0	0	0	0
41	Long	G +	4.5	2.8	2.3	1.2	2.0	1.0	.7	2.0	0	.2	0	0
42	Long	G +	4.9	2.9	2.4	.3	2.2	.8	1.6	1.9	.1	.1	0	0
56	Long	G —	3.2	2.4	2.5	2.2	1.5	0	0	.1	0	0	0	0
67	Short	G +	1.2	1.2	2.6	2.6	.7	1.7	..	..	.1	.1	0	0
70	Long	G —	4.6	1.2	4.5	.4	2.3	1.2	2.1	.3	0	0	0	0
71	Long	G ±	4.5	4.0	4.2	.5	2.0	1.0	2.0	2.0	0	0	0	0
72	Long	G ±	4.2	3.5	4.3	.5	2.4	1.0	2.1	2.0	.1	.2	0	0
73	Long	G —	4.8	3.6	4.4	0	2.2	1.3	2.2	1.9	.1	.1	0	0

*Maltose*: The throat cultures show a distinct reaction mode, falling between 1.0 and 1.5 per cent. acid. As in the case of lactose, the streptococci from milk are most adaptable as regards their temperature relations.

*Saccharose*: In this sugar the milk cultures readily produce 2 per cent. acid at 20 C., while the throat strains seldom give more than 0.5 per cent. Reference to Chart 3 shows strikingly this distinction. No other features worthy of particular note are brought out by the 37 degree reactions.

*Raffinose*: This trisaccharid was rarely fermented and when a reaction was present it was very feeble as shown by reference to the tables.

*Mannite*: Only a single culture was capable of producing as much as 0.4 per cent. acid with the alcohol mannite. It is obviously of little diagnostic value with throat or milk streptococci.

The results from the cultures isolated from "abnormal" throats showed no essential differences from the normal throat streptococci.

No clue to the relationship of the forms studied was obtained from either morphologic or staining characteristics.

#### CONCLUSIONS

Our work leads us to make the following tentative conclusions:

1. Streptococci from the human throat and from fresh milk very generally ferment one or more of the sugars, dextrose, lactose, maltose and saccharose, attacking them most readily in the order named. They do not generally ferment raffinose or mannite.
2. The streptococci of the sore throat and the normal throat show no cultural differentiation in relation to the carbohydrates used. Virulence tests might have separated the two groups.
3. The throat streptococci do not readily ferment at 20 C. any of the sugars used, while the milk organisms attack the same sugars and to the same extent at this temperature as at 37 C. This is, perhaps, the most valuable differential feature between chained cocci from these two sources.

#### BIBLIOGRAPHY

1. Gordon, M. H.: Thirty-third An. Rep. Loc. Gov. Board, 1905.
2. Houston, A. C.: Rep. London County Council, 1905.
3. Andrews, F. W., and Horder, T. J.: Lancet, London, 1906, clxxi, 708.
4. Winslow and Rogers: Relationships of the Coccaceæ, 1910.
5. Winslow and Palmer: Jour. Inf. Dis., 1910, vii, No. 1.
6. Gordon, M. H.: Fortieth An. Rep. Loc. Gov. Board, 1910-1911.
7. Broadhurst, J.: Science, 1912, xxxv, No. 893.
8. Winslow: Ibid.
9. Howe, E. C.: Ibid.
10. Stowell and Hilliard: Ibid.
11. Jackson, D. D.: Jour. Am. Pub. Health Assn., 1912, i, No. 12.

## THE EFFECT OF COLD FRESH AIR ON THE BLOOD-PRESSURE IN PNEUMONIA OF CHILDREN \*

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It is the general impression of those who have treated children with pneumonia out of doors, or in cold rooms with good ventilation, that, in addition to the increased quiet of the patients and their greater tendency to sleep, the circulatory system is not so profoundly affected and stimulation is less frequently required. Any positive evidence in regard to these impressions has been, however, so far as we are aware, lacking.

In a study of the effects of various circulatory stimulants it was found that a child of 5 years with a febrile pneumonia who received a subcutaneous injection of 1 grain of camphor immediately after being brought in from a balcony in winter, suffered no rise in blood-pressure such as would be expected from the camphor, but on the contrary a decided fall and this fall continued for an hour. As a result of this experience it was decided to test the effect of cold fresh air on the blood-pressure of children with pneumonia and of those convalescing from the disease.

The determination of the blood-pressure of children under 2 years of age by any method involving palpation of the radial artery is so unsatisfactory that the results are usually almost worthless. The children are likely to be so much disturbed as to make the value of any reading uncertain, the arteries are difficult to palpate especially if the pressure is low and the usual cuff is altogether too large. Our results were obtained with a Faught sphygmomanometer which gives very accurate but, we believe, somewhat higher readings than other instruments of the same general type. It allows the point of obliteration of the radial pulse to be determined with great accuracy. This was found to be more reliable than the point of return of the pulse. The reading was always repeated. A special cuff narrower than those usually employed was used. This was rendered necessary by the size of many of the children. The personal element always enters somewhat into the use of instruments of the Riva-Rocci type but with the method which we have employed the variations due to different observers were very slight; in all cases, however, the pressures of each child were read by the same person. No determinations were made unless the child was absolutely quiet and unaffected by the manipulation. The influence of excitement and muscular exertion

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\*From the Children's Service of the First Medical Division, Bellevue Hospital, New York.



may, therefore, be eliminated. The readings reported are those of the systolic pressure.

There is even more uncertainty as to the average blood-pressure of normal children at the various ages than as to the average pressure of normal adults, and for very obvious reasons. Taking the observations of Wolfensohn-Kriss,<sup>1</sup> Kaupé,<sup>2</sup> Beretta<sup>3</sup> and Oppenheimer and Bauchwitz,<sup>4</sup> we may consider that the averages are fairly well represented by the following figures:

Age, Years	Blood-Pressure, mm.	Age, Years	Blood-Pressure, mm.
1/12-1	75- 80	5-8	90- 95
1-3	80- 85	8-10	95-100
3-5	85- 90	10-12	100-105

### PNEUMONIA

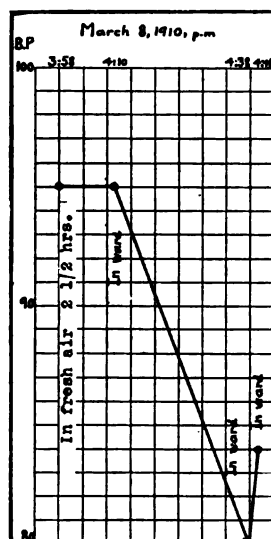


Chart 1.—F. K., aged 8 years. Severe lobar pneumonia and beginning empyema. Operation two weeks later. Recovery. Each square represents five minutes.

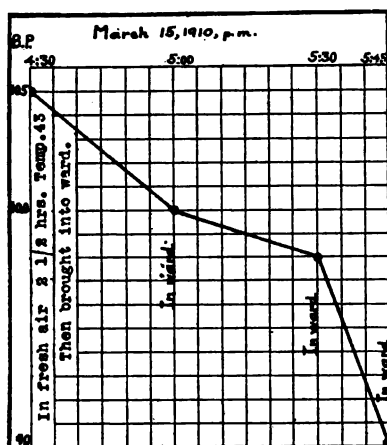


Chart 2.—A. M., aged 25 months. Mild bronchopneumonia. Temperature never above 102.5 F. (39.2 C.). Recovery. Each square represents five minutes.

As already stated, we believe that the Faught instrument in the hands of those accustomed to its use gives readings as a rule from 5 to 10 mm. higher than most instruments of the Riva-Rocci type and that averages with this instrument would probably be a little higher than the figures

1. Wolfensohn-Kriss: *Archiv. f. Kinderh.*, 1910, liii, 332.
2. Kaupé: *Monatschr. f. Kinderh.*, 1910, 257.
3. Beretta: Quoted by Oppenheimer.
4. Oppenheimer and Bauchwitz: *Arch. f. Kinderh.*, 1906, xlii, 415.

given. There are, however, marked exceptions to these averages, chiefly on the high side, and it is not unusual to find the blood-pressure of a child 10 or 15 mm. of mercury higher than that of other children of the same age and development. These factors, however, do not influence the value of the variations which are brought about by the influence of cold fresh air, as it is the relative and not the absolute pressure that is of interest.

Studies of the blood-pressure in pneumonia have not allowed the formulation of any definite rules in regard to its behavior. The great

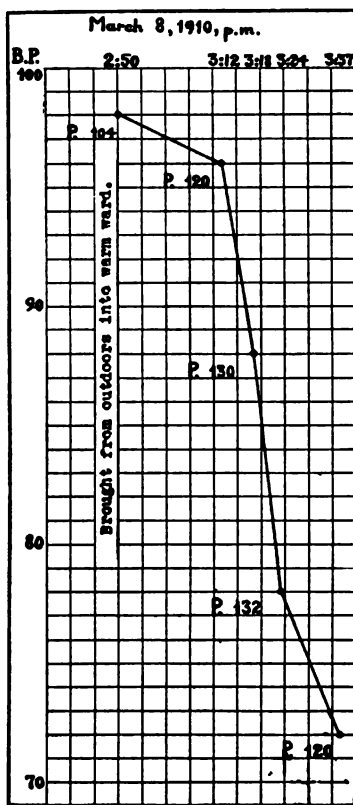


Chart 3.—F. F., aged 5 years. Prolonged extensive bronchopneumonia. Died March 25. Each square represents five minutes.

majority of observations have been made on adults, and irregularly, only one or two in the course of a day, with a great variety of instruments, and very seldom have control readings been made when convalescence has been completed. It is believed by Cook and Briggs,<sup>5</sup> Trumpp<sup>6</sup> and

5. Cook and Briggs: Johns Hopkins Hospital Reports: 1903, xi, 451.

6. Trumpp: Jahrb. f. Kinderh., 1906, lxiii, 43.

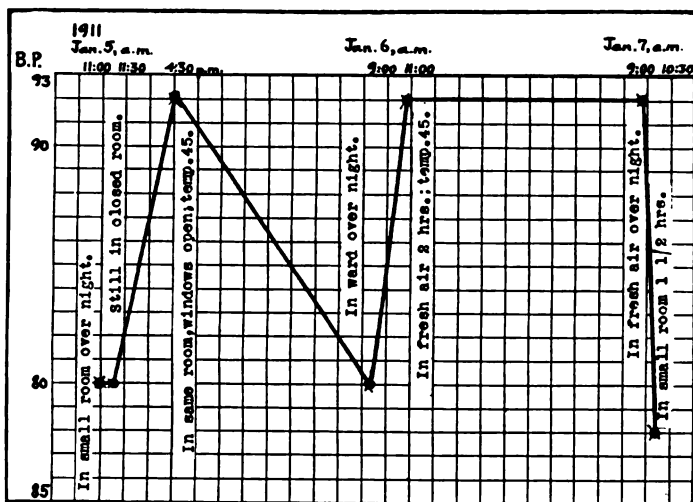


Chart 4.—M. B., aged 2 years. Prolonged severe bronchopneumonia. In hospital from Nov. 10, 1910, to Jan. 10, 1911. Taken home against advice. Each square represents two hours.

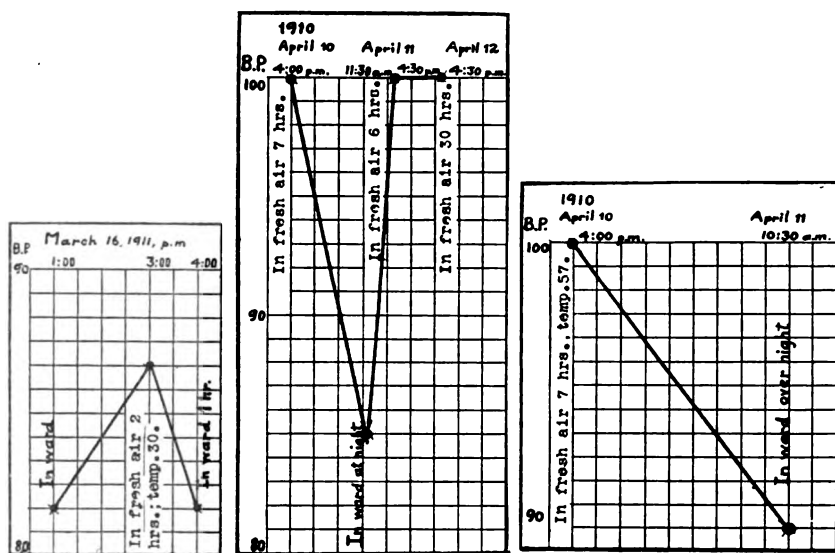


Chart 5.—R. F., aged 6 years. Moderately severe lobar pneumonia, defervescing by lysis on March 18. Each square represents one-half hour.

Chart 6.—T. P., aged 2½ years. Sharp attack of bronchopneumonia. Temperature normal on April 12. Each square represents six hours.

Chart 7.—C. M., aged 4 years. Bronchopneumonia with very irregular temperature. Defervescence by lysis on April 10. Each square represents two hours.

Muggia<sup>7</sup> that there is an increase in the blood-pressure, especially of children, unless the patients are in collapse. Kaufmann and de Bary,<sup>8</sup> Rongier,<sup>9</sup> Carter,<sup>10</sup> Durand-Viel,<sup>11</sup> Ambard and Beaujour,<sup>12</sup> Ekgren,<sup>13</sup> Külbs<sup>14</sup> and Gilbert and Castaigne<sup>15</sup> believe that the pressure is in general lowered and that it may diminish markedly and suddenly at the time of crisis. Our observations were not made with the object of testing this point, but it is apparent that children seriously ill as were Patients 1, 3, 5, 8 and 10, may have, at ordinary room temperatures, a blood-pressure somewhat below what might be expected at that age. This point can only be determined by a great number of readings carried out throughout the course of the disease.

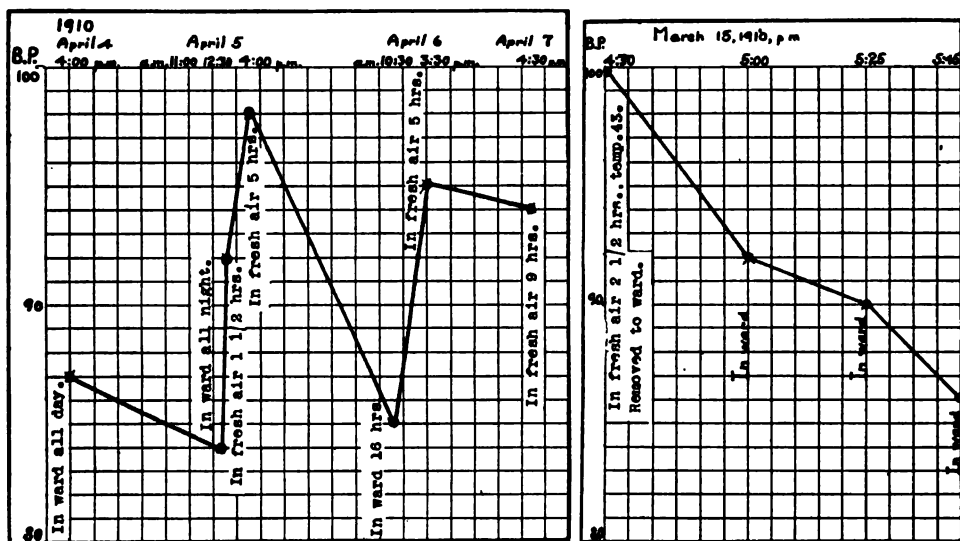


Chart 8.—S. B., aged 8 years. Frank lobar pneumonia. Defervescence by crisis on April 6. Each square represents three hours.

Chart 9.—M. L., aged 2 years. Bronchopneumonia. Defervescence by crisis March 16. Each square represents five minutes.

Our patients were treated in the wards of Bellevue Hospital, which are thoroughly ventilated and usually kept at a temperature of about 65 F. (18 C.), or on the balconies outside of the wards. In the wards

7. Muggia: Quoted by Beretta.

8. Kaufmann and de Bary: *Berliner klin. Wehnschr.*, 1888, xxv, 557.

9. Rongier: *Thèse de Paris*, 1900.

10. Carter: *Am. Jour. Med. Sc.*, 1901, cxxii, ii, 854.

11. Durand-Viel: *Thèse de Paris*, 1903.

12. Ambard and Beaujour: *Arch. gén. de méd.*, 1904, i, 520.

13. Ekgren: *Zeitschr. f. klin. Med.*, 1905, lvii, 411.

14. Külbs: *Deutsch. Arch. f. klin. Med.*, 1907, lxxix, 457.

15. Gilbert and Castaigne: *Rév. gén. de clin. et de pract.*, 1899, xiii, 769.

they were covered lightly with blankets; outside they were clothed in woolen wrappers and covered with many blankets, according to the temperature. Hot water bottles were at their feet and they wore hoods. Only the faces were exposed. None was receiving circulatory stimulation at the time that the readings were made. The accompanying charts show some of the results on the blood-pressure in children divided into two classes—the heading “pneumonia” indicating that they were still suffering from the disease and were in the febrile stage, and “convalescent” that they had defervesced, although not necessarily free from pulmonary signs.

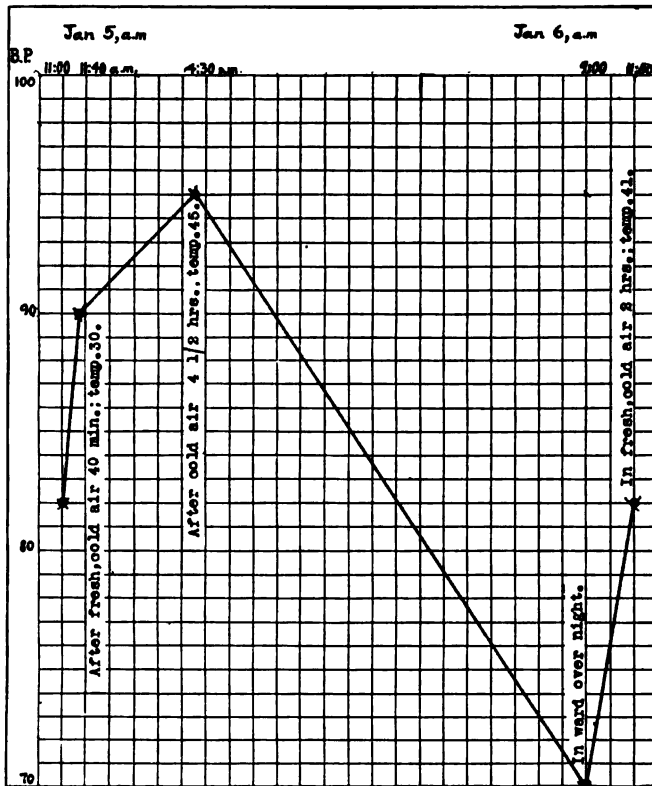


Chart 10.—H. G., aged 3 years. Lobar pneumonia running a severe course. Temperature normal on January 7. Each square represents one hour.

It will be seen from an examination of the charts that the effect of cold fresh air in patients with active pneumonia was always to produce a rise in blood-pressure and that removal to a warm but well-ventilated ward was to produce a fall in blood-pressure. We have never found this to fail, although in one or two instances the variation in pressure has not been as noticeable as in most of the charts shown. The rise is not apparent until half an hour or more, sometimes not until an hour, after

being put out of doors, and it does not reach its maximum for about two hours. Thereafter the effect, so far as we have observed, is continuous for even as long as thirty hours and we have not observed any tendency for the pressure to fall as if from exhaustion of the effect. We have not made observations on any fatal cases that were treated continuously out of doors and are therefore unable to say what would be the behavior of the blood-pressure in cases growing constantly worse and progressing to a fatal termination.

## CONVALESCENT

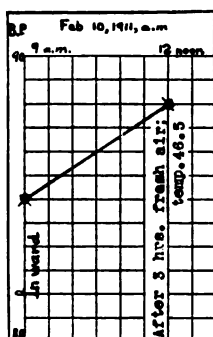


Chart 11.—M. B., aged 18 months. Two weeks after pneumonia. Each square represents one-half hour.

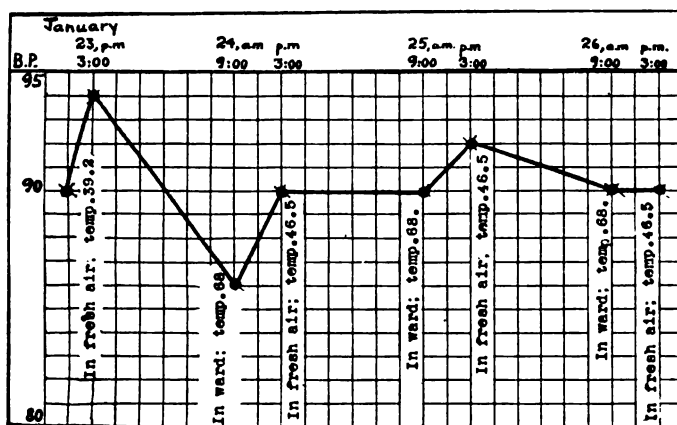


Chart 12.—C. H., aged 10 years. Moderately severe lobar pneumonia. Temperature normal for ten days. Each square represents three hours.

On the other hand, after removal from the cold fresh air the blood-pressure falls rapidly; the fall is apparent in fifteen or twenty minutes and usually reaches its lowest point in an hour, to remain at this minimum unless influenced by the course of the disease, by stimulation, or by the child's again being placed out of doors, when it again rises.

In convalescents, on the contrary, the results are usually much less striking and may even be absent. Instead of a rise of 10 or 15 mm. of mercury, the difference is only a few millimeters or none at all.

Chart 15 is an exception and shows as great an effect as is found during the acute febrile period. The pressure in the ward was 80 mm., or about 10 mm. less than would be expected in health. Whether this low pressure, which is occasionally found in convalescence, as is mentioned by Weigert<sup>16</sup> and other authors, can be thus influenced, in contradistinction to the pressure which is at or near normal, must remain undecided until a far greater number of observations can be made. We believe that it is very likely that this is the case.

The number of our observations have not been sufficiently numerous to allow us to say whether those children with a very low blood-pressure respond better than those whose pressure is nearly normal.

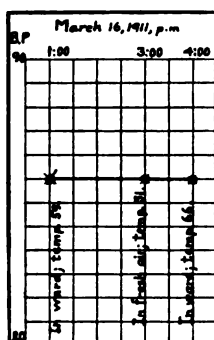


Chart 13.—D. W., aged 18 months. Had defervesced on March 15 after a mild attack of bronchopneumonia.

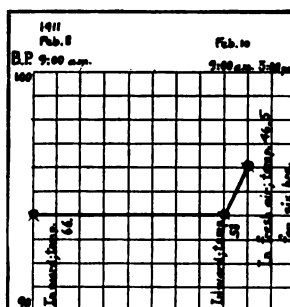


Chart 14.—B. A., aged 9 years. Mild lobar pneumonia. Defervescence by lysis. Temperature normal February 7. Each square represents six hours.

We have been unable to produce results by putting children out of doors in warm weather; as the temperature increases in the spring and the out-of-doors temperature approaches that of the ward, the effects are less and less marked until none whatever is produced. It would seem, therefore, that the all important factor is the cold.

The influence on the blood-pressure is undoubtedly brought about by reflex stimulation of the vasomotor center by the action of cold air on the skin of the face and on the nasal mucous membrane. No other part of the child is exposed and there is no additional factor that can be supposed to play a part. It is striking that this reflex should produce such a constant and continuous effect. As has been shown, the pressure remains at a higher level for hours, shows no tendency to fall and even

16. Weigert: Samml. klin. Vortr., 1907, Innere medizin, 138.

after a return to the ward does not fall to a point below that previously obtaining at the ward temperature.

As to the beneficial effect of cold air on the circulation, there can be no doubt that when the pressure is abnormally low an increase in this, which is accomplished without disturbance or irritation, which is constant and continuous and which causes no exhaustion or bad effects, is of the greatest value. We are quite aware that the determination of the blood-pressure alone does not give all the data in regard to the circulation, such as the mass movement of blood, etc., but taken with the ordinary methods of physical examination it is the best indication of the condition of the circulation that we possess. Chart 3 raises the question whether the cold by increasing the pressure to 98 mm. lessened the demands on the heart,

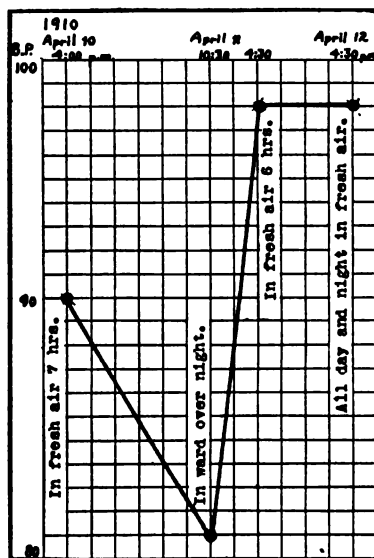


Chart 15.—A. S., aged 5 years. Lobar pneumonia, moderately severe. Temperature normal April 9. Each square represents three hours.

as indicated by a pulse-rate of 104, and whether the withdrawal of cold with the consequent fall of pressure to 72 demanded an increase of cardiac exertion, as indicated by a rise of the pulse to from 120 to 132. This leaves entirely out of account the other beneficial effects of cold fresh air.

The symptoms of the death of children from pneumonia are those of vasomotor failure. It is rare to see intense cyanosis, edema of the lungs and evidences of right heart incompetency. Whether under such circumstances cold air would have an influence in assisting the circulation we are unable to say.



Whether it is advantageous from the standpoint of the circulation to raise a blood-pressure which is at an average point or slightly above this is a question which we cannot at this time answer. It may be that the pressure is only maintained at this point by an unnecessary cardiac exertion accompanied by a very rapid pulse and that a high pressure, reflexly produced through the vasomotor system, may allow of greater rest to the heart. We are confident that we have observed no bad effects on the circulation nor have any been reported, notwithstanding the prevalence of the cold air treatment of pneumonia and the lack of selection of patients to be treated by this method. It is possible that from the beginning of the disease when the blood-pressure is not low, cold air may have a beneficial tonic action on the vasomotor center so as to render it less likely to be profoundly influenced by the organisms or their products, and it seems to us very likely that the other beneficial effects of cold air may so modify the disease as to render less likely the development of partial or complete circulatory failure.

## A STUDY OF ICTERUS NEONATORUM BY MEANS OF THE DUODENAL CATHETER \*

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The occurrence of jaundice within the first few days of life has, as might be expected, stimulated repeated investigation. The theories advanced to account for this striking phenomenon have been most ingenious, but being based quite as much on speculation as on fact, they have proved unsatisfactory and have been accepted only tentatively in lieu of something sounder. The excuse offered for entering on a path so well trodden is that a new point of vantage of this subject now presents itself, through the use of the duodenal catheter, recently described in quite another connection in the pages of this journal.<sup>1</sup> By this means direct access to the bile is afforded at its site of excretion. Before presenting the data gathered by this means, however, it would seem of advantage to sketch in outline the present status of this question.

It is to be noted at the outset that there is a surprising lack of unanimity even as to the incidence of icterus neonatorum. This is all the more remarkable when we consider that this phenomenon is of so simple a nature that it should not allow of a wide variance of opinion. Nevertheless we find the incidence given by some as 15 per cent., by others as 85 per cent., and by still others placed at various levels between these extremes. This marked divergence must be attributed almost entirely to differences in method of examination. It would seem that those who made a point of examining with the aid of strong daylight, and of looking for the faint yellow tinge on the back or on the nostrils, rather than in the sclera, as in the case of adults, have observed icterus in at least 75 per cent. of infants. In a series of 100 infants whom I examined for this sign, it was definitely noted eighty-three times. But even this figure probably does not give us a correct idea of its frequency, for it is manifestly impossible for us to detect by means of mere clinical inspection the presence of a trace of bile in the blood or in the skin, and when we consider the crudeness of the test, and remember that bilirubin crystals frequently have been found in the tissues of infants who showed no jaundice during life, <sup>2, 3</sup> we probably do not err in believing that there are few instances in which bile does not enter the general circulation

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\*From the Research Laboratory, Board of Health, New York City.

1. Hess, A. F.: *AM. JOUR. DIS. CHILD.*, March, 1912.

2. Neumann, E.: *Virchows Arch. f. path. Anat.*, 1888, cxiv, 394.

3. Orth, J.: *Virchows Arch. f. path. Anat.*, 1875, lxiii, 446.

soon after birth. In view of its frequency, icterus neonatorum must therefore be considered a peculiar entity, the sole example of a physiologic icterus.

The opinion that this icterus is hematogenic in origin, that the bile is formed directly from the blood pigment, does not need more than passing mention, since it was proved experimentally by Minkowski and Naunyn<sup>4</sup> and by others that if the liver is extirpated jaundice cannot be induced; and since Birch-Hirschfeld<sup>5</sup> demonstrated bile acids in the pericardial fluid of infants who had manifested icterus neonatorum during life. The blood may likewise play a rôle in the causation of this form of jaundice. The presence of bile acids in the body fluids, however, conclusively showed the participation of the liver.

Although the hematogenic theory is certainly insufficient to account for this form of icterus, or indeed for any icterus whatsoever, it has been accorded a position of varying importance by many writers who believe in the hemohepato-genic origin of this disturbance. Hofmeier<sup>6</sup> was the first to advance the theory that in the new-born there is a marked destruction of red blood-cells in the circulation, that in cases of icterus neonatorum this takes place to an exceptional degree, and that hemoglobin thus set free forms the basis for an excess of bile formation in the liver (polycholic or pleiochromic icterus). Knöpfelmacher<sup>7</sup> has failed to find this destruction of red blood-cells and therefore gives this theory no place in the etiology of this form of icterus. However, very recently<sup>8</sup> blood examinations have again been reported to uphold it. In view of the fact that great weight has been attached to this etiologic factor, we should bear in mind that free hemoglobin has never been found in the new-born in the circulating blood. And what is of far greater moment in controverting the claim that this hemolysis is alone sufficient to account for the icterus is the experimental evidence that jaundice cannot be produced by intravenous injections of hemoglobin, and the clinical experience that it does not supervene following transfusion of blood.

Another theory which cannot be passed by without mention, as it prevailed for many years, was that of Frerichs.<sup>9</sup> The distinguished author of "Diseases of the Liver" explained this jaundice by reasoning that coincident with birth, and closely following the circulatory changes in the umbilical vessels, there results a marked anemia and decrease in pressure in the liver capillaries, which in turn leads to a diminished pressure in the bile capillaries, and an overflow of bile into the blood stream. Quite apart from the fact that this explanation is purely hypothetical, it can

4. Minkowski and Naunyn: *Arch. f. exper. Path. u. Pharmacol.*, 1885, xix, 34.

5. Birch-Hirschfeld: *Virchows Arch. f. path. Anat.*, 1882, lxxxvii, 1.

6. Hofmeier: *Ztschr. f. Geburtsh. und Gynäk.*, 1882, viii, 287.

7. Knöpfelmacher, W.: *Wien. klin. Wchnschr.*, 1896, No. 43.

8. Heimann, F.: *Ztschr. f. Geburtsh. und Gynäk.*, 1912, lxxix, 165.

9. Frerichs: *Klinik d. Leberkrankh.*, 1858, i, 198.

no longer be given any weight, in view of the marked congestion of the hepatic vessels, in contradistinction to an anemia which has been uniformly found at autopsy of the new-born.

The theory to-day which, according to Finkelstein,<sup>10</sup> finds the greatest acceptance is that of Quincke.<sup>11</sup> This author believes the patency of the ductus venosus to be the deciding etiologic factor. If this connecting link between the portal and systemic venous circulation fails of obliteration at birth, icterus results, as bile passes directly from the meconium in the intestine to the portal vein, and circumventing the liver, enters the inferior vena cava. There are other subsidiary causes which play a part, such as the polycholia, the small amount of bile pigment excreted by the kidneys, and the peculiar nature of the intestinal contents, the bile containing meconium. As this theory enjoys such wide acceptance, it demands particular consideration, and it is therefore remarkable that although it was promulgated some twenty-seven years ago, so little experimental work has been undertaken to confirm or refute its validity. Quincke himself investigated the condition of the ductus venosus in only five cases, and in these reported on the circumference of the vein rather than on its lumen, which would seem to be the more important factor. Schreiber<sup>12</sup> supported this theory by citing the figures of patency of the ductus venosus published by Elsässer<sup>13</sup> many years ago. However, these figures may well be used against Quincke's hypothesis. In ninety-two autopsies on infants born alive, the ductus venosus was found patent in sixty-five, and in fifty of these where the infant was seven days or more of age, the ductus was patent in thirty-one and closed in nineteen instances. This includes some premature infants, and omits some cases in which post-mortem conditions seem insufficiently described. In the second week of life the ductus was patent in nineteen out of twenty-seven cases, in the third week in eight out of fifteen cases, and also in four of eight dissections made at a still later period of life. It is needless to add that if we use this anatomic study as a criterion, we should not be led to consider this icterus as a consequence of a patent ductus venosus; for if such were the case, icterus neonatorum would be a phenomenon not of the first week but of the first month of life.

It should be remembered that Elsässer carried out this investigation purely for medicolegal purposes. There has been no investigation to correlate anatomic findings of this nature with the clinical occurrence of icterus, and without this link these mere dissections can furnish but inconclusive evidence. It would seem worth while to study the patency

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10. Finkelstein, H.: *Lehrbuch d. Säuglingskrankh.*, 1905, i.

11. Quincke, H.: *Arch. f. exper. Path. u. Pharmacol.*, 1885, xix, 34.

12. Schreiber, E.: *Berl. klin. Wchnschr.*, 1895.

13. Elsässer: *Ztschr. f. Staatsarzneikunde*, 1841, xli.

of the ductus venosus also in animals and to determine whether it bears any relation to jaundice.

Knöpfelmacher<sup>14</sup> probed this theory by attempting to remove the meconium from the bowel shortly after birth. With this end in view he used repeated high enemata, employing acidulated water in order not to dissolve the bilirubin, and performed four to eight irrigations of this nature. Although this method is ingenious, its results do not seem conclusive; for on scanning the notes of the twenty cases on which this experiment was carried out, it is evident that the bowel was not completely emptied of meconium. In most cases a "milk-stool" did not appear until the third or the fourth day of life, which must entirely invalidate the test. Furthermore, only one case is noted in which jaundice made its appearance later than the milk-stool, and on this point the entire experiment would seem to hinge—the occurrence of jaundice after and in spite of the emptying of the intestine of all meconium. The question does not seem to be open to solution by this method, for it is impossible to be certain that meconium is not still present in the bowel. Indeed, in this connection Kehrers's<sup>15</sup> figures showing that the jaundice bears no relation to the date of disappearance of the meconium, and the appearance of "milk-stools," and that among his 123 cases, when the yellow stools appeared late there was no increased frequency or intensity of jaundice, seem quite as convincing as Knöpfelmacher's carefully planned experiment.

There are many other theories which might well be mentioned, but we shall limit ourselves to an outline of a group which may be designated as that of bile stasis. It is unnecessary to consider such hypotheses as an obstruction of the bile-ducts by mucus or epithelium (Virchow), or a congenital narrowness of these ducts (Kehrers), or compression of the larger ducts through edema of Glisson's capsule, as post-mortem examination has failed in every instance to confirm them. There are other investigators, however, who believe that this stasis of bile results from inadequate excretion, that the bile is forced out of the intracellular biliary capillaries into the liver cells and then enters the blood stream. Browitz<sup>16</sup> has supported this theory with careful microscopic examinations which have been confirmed by Knöpfelmacher. Neither believes that the jaundice is due to mechanical obstruction, as no tears in the fine bile ducts are found, merely varicosities, but rather to a disturbance of function of the liver cells allowing a reverse current of bile into the blood stream. In stillborn infants Knöpfelmacher<sup>14</sup> describes an increased viscosity of the bile, but in infants of the first few days of life a markedly decreased viscosity with an abnormal distention of the bile capillaries. The viscosity

14. Knöpfelmacher, W.: *Jahrb. f. Kinderh.*, 1908, lxvii, 36.

15. Kehrers: *Oesterr. Jahrb. f. Pädiat.*, Wien, 1871, p. 71.

16. Brewitz: *Wien. klin. Wchnschr.*, 1900, p. 785.

tests were carried out according to Ostwald's method. However, the bile was obtained from the gall-bladder and not from the hepatic ducts, and may have been a fetal secretion. The histologic investigations showing bile stasis are especially welcome, as they do not burden the already over-weighted etiology of icterus neonatorum with another theory.

#### INVESTIGATION WITH DUODENAL CATHETER

It is possible to pass the duodenal catheter in the new-born infant with as great ease as in infants a few months of age. The technic is the same; however, a 14 (F.) Nélaton catheter is used instead of the larger 15 (F.) catheter. There is a tendency to slight bleeding due to the delicate texture of the mucous membrane during the first hours and days of life, and for this reason aspiration must be gentle.

It seemed that the first point to ascertain should be the time when excretion of bile begins in the new-born. Accordingly the catheter was passed on infants a few hours old; indeed, in four cases within two hours of birth. It is advisable from an etiologic point of view to divide the cases into groups, those tested before they had nursed, and those tested subsequent to nursing. The former group comprises fifty-two cases, almost all under 6 hours old, the time when the infant was usually put to the breast. It includes, however, in addition to four infants under 2 hours old, several 12 hours old. The test was carried out generally in two stages, and the catheter was passed into the duodenum in the manner previously described, and after ten minutes of intermittent aspiration withdrawn; it was then washed out and reintroduced for the same length of time. Dividing the test in this way has the advantage of avoiding an error which might be occasioned by the plugging of the lumen of the catheter with mucus, an event which would of course nullify the test if it occurred soon after the intestine was entered. It is of further advantage, at it happens frequently in the new-born, owing to the pressure of the pyloric or cardiac sphincter, that it is impossible to aspirate viscid fluid, and the bile or intestinal juice is obtained only after the catheter is withdrawn into the stomach or even into the esophagus. For these reasons the two tests furnish a safer criterion. Where any doubt as to the reliability of the test was entertained, aspiration was continued for a longer period.

Bile was obtained but once in the course of these fifty-two tests, and in that instance in small quantity from an infant  $2\frac{1}{2}$  hours old (Table 1). It may therefore be stated that in the first half day of life there is rarely an excretion of bile into the intestine. It is possible, had the test been continued for many hours, a procedure which did not seem justifiable, bile might have been oftener encountered. However, the aspirations were sufficiently numerous to warrant the deduction that bile, in general, is not excreted during this early period.

Nineteen tests were made on infants from 12 to 36 hours old. It was found that where marked jaundice was present, in four cases, bile could be obtained, but that where it was absent, in fifteen cases, bile also was absent. Mere statistics, therefore, cannot give a correct idea of the bile excretion of this period, for they will vary according to the number of cases of marked jaundice which they comprise. This is true to some extent in infants  $1\frac{1}{2}$  to 3 days old. As the infants increased in age I found bile in increasing frequency; never to the same extent, however, as in the deeply jaundiced infant (Table 1). There is no doubt that in some instances although bile was not obtained, it must have been excreted to some extent into the gut. This was to be expected when we consider that although bile is secreted continuously it is excreted intermittently. In this connection we may refer to Table 2, composed of cases in which numerous tests were carried out on the same infants on consecutive days. A survey of this table shows that when bile was obtained it was almost always found in successive examinations, and that its presence was not subject to caprice.

TABLE 1.—RELATION OF AGE TO EXCRETION OF BILE (DUODENAL CATHETER)

No. of Cases	Age	No Bile	Bile	Marked Jaundice	Remarks
52	$\frac{1}{2}$ -12 hrs.	51	1	0	39 cases were less than 6 hours old.
19	12-36 hrs.	15	4	4	Marked jaundice in all four positive cases; in others no bile obtained.
15	$1\frac{1}{2}$ - 3 days	5	10	6	Marked jaundice in four positive cases; in other two jaundiced cases bile next day.
13	3- 4 days	4	9	6	Jaundice not increasing.
12	4- 5 days	2	10	5	Jaundice decreasing.
13	6-11 days	2	11	4	Jaundice decreasing.
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124					

In twenty-four cases a careful study was carried out of the relation of the bile excretion to jaundice. In some of these cases the catheter was employed in a routine manner soon after birth, and then every day subsequently until bile was obtained on two successive occasions. These infants were unselected. In eleven of the cases, however, a selection was made, based on the occurrence of early or marked jaundice. Seventy-two tests in all were carried out, the results of which are given in Table 2 (a) (b). A most striking and consistent fact was that bile was not obtained in any case previous to the appearance of jaundice. Even where bile was obtained within the first twenty-four hours, a marked early jaundice also manifested itself (Cases 9 and 19). It is evident that the quantity of bile secreted plays an important rôle. In one case (Case 3), for example, excretion was delayed, and bile was not obtained until the seventh test, so that unless secretion of bile had been exceptionally meager, this certainly must have resulted in marked icterus. On the contrary, a slight ephemeral jaundice was noted on the second day. And again if we

TABLE 2.—RELATION OF JAUNDICE TO BILE EXCRETION (DUODENAL CATHETER)

(A) *Unselected Cases*

Case	Age, Days	Bile*	Jaundice	Food Supply	Remarks
1	$\frac{5}{8}$	—	0	Colostrum +	
	$2\frac{5}{8}$	+	+	.....	
	$3\frac{5}{8}$	0	++	.....	
	$4\frac{5}{8}$	0	—	.....	
2	$\frac{1}{8}$	—	—	Colostrum +	
	$1\frac{1}{8}$	—	+	Colostrum +	
	$2\frac{1}{8}$	—	++	Colostrum ++	
	$3\frac{1}{8}$	+	++	Milk +	Ten-minute test.
	$4\frac{1}{8}$	+	++	.....	Ten-minute test.
3	$\frac{1}{4}$	—	—	Not fed.	
	$1\frac{1}{4}$	—	+	Colostrum +	
	$2\frac{1}{4}$	—	—	Colostrum ++	
	$3\frac{1}{4}$	—	—	Colostrum ++	
	$4\frac{1}{4}$	—	—	Milk.	
	$5\frac{1}{4}$	—	—	.....	Bile in stool
	$6\frac{1}{4}$	+	—	.....	Ten-minute test.
	$7\frac{1}{4}$	—	—	.....	Castor-oil given shortly before test.
	$8\frac{1}{4}$	+	—	.....	Five-minute test.
4	$\frac{1}{4}$	—	—	Not fed.	
	$1\frac{1}{4}$	—	—	Colostrum —	Ten-minute test.
	$2\frac{1}{4}$	+	—	Milk.	
5	$\frac{1}{8}$	—	—	Not fed.	
	$1\frac{1}{8}$	—	+	Colostrum +	
	$2\frac{1}{8}$	—	++	Colostrum ++	
	$3\frac{1}{8}$	+	++	Milk.	Bile in second test.
	$4\frac{1}{8}$	+	++	.....	Bile in both tests.
6	$6\frac{1}{8}$	0	++	.....	
	1	—	+	.....	Supplementary feed-ings begun at one hour.
	2	—	—	.....	
	3	—	—	.....	
7	4	+	—	.....	
	$\frac{1}{4}$	—	+	Not fed.	
	$1\frac{1}{4}$	—	+	Colostrum +	
	$2\frac{1}{4}$	+	+	Milk.	Bile in both tests.
8	$3\frac{1}{4}$	+	++	.....	Bile obtained at once.
	$\frac{1}{8}$	—	—	.....	
	$1\frac{1}{8}$	—	+	.....	
9	$2\frac{1}{8}$	+	±	.....	
	1	+	+	.....	Bile in second test.
	2	++	++	.....	Bile in first and second test.
10	$\frac{1}{2}$	—	—	.....	Weight 6 lbs. 13 oz.
	$1\frac{1}{2}$	—	+	.....	Weight 6 lbs. 10 oz.
	$3\frac{1}{2}$	—	+++	.....	Weight 6 lbs. 9 oz.
	$4\frac{1}{2}$	—	+++	.....	Weight 6 lbs. 10 oz.
	$5\frac{1}{2}$	+	+++	.....	Weight 6 lbs. 11½ oz.
	$6\frac{1}{2}$	+	++	.....	Ten-minute test.
11	$6\frac{1}{2}$	+	++	.....	Weight 6 lbs. 13½ oz.
	$11\frac{1}{2}$	—	+	.....	Ten-minute test.
12	$1\frac{1}{8}$	—	—	.....	Early jaundice,
	$1\frac{1}{8}$	—	—	.....	Supplementary feeding begun at two hours.



TABLE 2.—Continued.

Case	Age, Days	Bile*	Jaundice	Food Supply	Remarks
13	3 $\frac{1}{8}$	+	++	.....	Bile in stomach.
	4 $\frac{1}{8}$	+	+	.....	Ten-minute test.
	1 $\frac{1}{4}$	—	+	.....	
	2 $\frac{1}{4}$	—	0	.....	
	3 $\frac{1}{4}$	—	—	.....	
	4 $\frac{1}{4}$	+	—	.....	Bile obtained at once.
	5 $\frac{1}{4}$	—	—	.....	

## (B) Cases Selected on Account of Early or Marked Jaundice

14	3 $\frac{3}{4}$	+++	+++	.....	Bile in stomach.
	4 $\frac{3}{4}$	0	++	.....	Bile in stomach.
15	4 $\frac{1}{2}$	+++	+++	.....	Bile in stomach. Two-minute test.
	5 $\frac{1}{2}$	..	++	.....	Bile in stomach. Two-minute test.
16	2	+++	+++	.....	A case of "Family Icterus." Infant saffron colored, skin dry, marked loss of weight, anuria. Bile in stomach at each test.
	3	+++	+++	.....	
	4	++	+++	.....	
	5	++	+++	.....	
	6	+	++	.....	
17	6	+	+++	.....	Jaundice decreasing.
18	3 $\frac{1}{2}$	+	++	.....	
	4 $\frac{1}{2}$	+	++	.....	Jaundice decreasing.
19	5/6	+	++	.....	
20	3 $\frac{1}{2}$	++	++	.....	Bile in stomach and vomitus.
21	1 $\frac{1}{2}$	++	++	.....	Bile in stomach and vomitus.
22	3	++	++	.....	Bile in stomach.
	4	++	+++	.....	Bile in stomach.
	5	++	++	.....	
23	6 $\frac{3}{4}$	+	+++	.....	Bile in stomach.
24	8 $\frac{1}{2}$	+	+++	.....	Jaundice decreasing.

\*+=Present; —=absent; 0=no examination.

compare a case in which there was no jaundice (Case 4), with another in which there was the most intense saffron jaundice, we find that in the latter instance the excretion of bile began earlier and was incomparably more profuse; indeed, in the jaundiced case the excretion of bile seemed almost continuous. Had the jaundice depended solely on the excretory function of the liver, the amount of bile secreted being the same, conditions must have been reversed. The importance of the secretion in this connection is further emphasized when we compare the columns of the table and note the general parallelism of marked jaundice and marked bile. And yet the efficiency of excretion also plays a part, for it is clear that if excretion were adequate there would be no stagnation of bile, and the dilatation of the biliary capillaries, which is a definite and constant histologic accompaniment of icterus neonatorum, would not occur. It has, furthermore, been repeatedly shown by animal experimentation that

jaundice cannot be effected, however greatly we may increase the secretion of bile, unless excretion is at the same time hampered. However, experiments of this nature on normal new-born animals would be of exceptional interest.

There are some other points noted in this table which require a word of explanation. In many of the cases a record was made of the time when colostrum appeared in the mother's breasts, of its profuseness, and of the day on which milk was first secreted. This was done with the purpose of ascertaining whether these facts bore any relationship to the occurrence of jaundice. In addition, a number of infants, some of whom are included in this table, were given colostrum within the first few hours of life, expressed from the breasts of mothers whose children were 2 to 3 days old. The object of these tests was to determine whether, as has been claimed, starvation of the infant during the first day or two of life is an etiologic factor of the icterus. It was soon evident that it was a consideration of little moment; in the case showing no jaundice, the colostrum was noticeably scanty (Case 4), whereas in an instance in which colostrum feeding was begun when the baby was 2 hours old, jaundice was marked (Case 12). Furthermore, jaundice developed in a baby which gained 7 ounces during the first four days, owing to the fact that the mother's milk was profuse almost immediately after delivery. These incidents also show that the occurrence of jaundice but once in the series of fifty-two infants who had not been fed, was due not to the lack of food but to their time of life. The weights of a number of infants have been recorded, as a loss has been emphasized by many writers. It is not exceptional, however, for an infant with marked jaundice to lose but a few ounces and to regain its birth weight within the first week (Case 4). We have not considered critically the bearing of prematurity, of asphyxia, and of breach presentations in the etiology. It has been interesting as well as instructive to note how the predominance of jaundice in these abnormal conditions has been brought forward to strengthen the most divergent theories, from that of Morgagni, who laid the burden on the diminished pressure in the hepatic circulation, to those of the present day.

#### SUMMARY

Tests by means of the duodenal catheter show that bile is very rarely excreted during the first twelve hours of life; it was obtained but once in the course of fifty-two tests.

Bile excretion during the subsequent twenty-four hours is variable; in cases of marked jaundice it is profuse; in cases not jaundiced it is scanty or absent.

The function of excretion gradually becomes fully established during the first week or ten days of life.

Where jaundice manifests itself, it precedes the excretion of bile into the duodenum.

Secretion of bile varies within wide limits. In general it is marked when the jaundice is marked.

The occurrence of jaundice results from a defective correlation of excretion and secretion. It is generally caused by the inability of the rudimentary excretion to cope with the sudden profuse secretion of bile.

#### CONCLUSIONS

Icterus neonatorum has always been the favorite domain of hypotheses, and happily I have no new theory to introduce into this overcrowded realm. It would seem beyond doubt that in most cases there is a disturbance of secretion, a polycholia, or according to Stadelman, a mere increase in the formation of bile pigment (pleiochylia). In many of the cases of marked jaundice this hypersecretion reaches an intensity so marked that bile overflows into the stomach, where it may be found on introducing the stomach tube, or manifests itself by its presence in the vomitus. The cause of this pleiochylia is not at present definitely proved, so that it would seem advisable in this instance to follow the principles of the physiology of bile secretion and assume, what seems probable, that it is due to an increased amount of available hemoglobin; that bile salts are absorbed from the intestine, resulting in a disintegration of blood-cells and a consequent increased elaboration of bile in the liver. Whether or not this explanation of its histogenesis prove correct does not alter the fact of the usual occurrence of a hypersecretion.

In addition to the disturbance of secretion there is a coincident disturbance of excretion, and it is probable that were excretion as well provided for at birth as in later infancy, there would be no disturbance such as icterus neonatorum. We find, however, that the liver is most inadequately equipped to excrete this excess of bile; that during the first hours of life there is practically no functioning excretory mechanism, and that this function manifests itself but gradually. The bile is secreted under low pressure, but where an excess is secreted, as is generally the case in jaundice, the pressure is proportionately increased, so that a profuse excretion of bile into the duodenum is obtained. Nevertheless, congestion of the biliary capillaries ensues, as is shown by histologic investigations, and icterus results.

There has been too little consideration of the interrelation of secretion and excretion. The former may be said to be the more important, for in some cases in which there is but slight secretion, the rudimentary excretory function suffices to prevent the manifestation of icterus. That the lack of excretion cannot be the sole cause of the disturbance is evident when we consider that several cases of congenital obliteration of the bile

ducts have been reported<sup>17</sup> in which icterus did not develop for days or even weeks, and yet this lesion may be considered comparable to the complete tying off of the common bile duct at birth. The complementary parts which secretion and excretion play in icterus neonatorum may well be compared to these functions in the breast after parturition. If the excretion of milk is copious and adequate, no pathologic phenomena result; however, if it prove inadequate, stasis ensues, lactose enters the blood stream and appears in the urine. The lactose is the counterpart of the bile. The reason why jaundice appears in the first days of life is because at the time when excretion has incompletely assumed its function throughout the body, in the liver as well as in other organs, for example, in the breasts and in the kidneys, a sudden flood of bile is poured into the passive excretory ducts and gains access to the hepatic circulation.

154 West Seventy-Second Street.

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17. Thomson, J.: Congenital Obliteration of the Bile Ducts, 1902.

## COMMUNICATION CONCERNING EIWEISSMILCH

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*To the Editor:*—In the November number of your journal in an article entitled “The Use of Malt Sugar and High Percentages of Casein in Infant Feeding,” Dr. Morse claims to have treated cases of nutritional disturbance in infants with a mixture based on the principles of eiweissmilch, and is not very well satisfied with the results. We, however, are still enthusiastic about eiweissmilch, having seen its success in hundreds of cases, and believe Dr. Morse’s conclusions may be due to an improper understanding of the technic and principles of feeding.

For example, on page 318, he says we advise giving 180 to 200 calories per kilo of body weight, and on page 326 that it is difficult to get children to take this amount. This is, of course, a gross error. We recommended not 180 to 200 calories, but 180 to 200 c.c. of eiweissmilch which, without addition of sugar, means only 70 calories per kilo.

In another place Dr. Morse says that we “seem to imply that all disturbances of nutrition occur independently of bacterial action.” We do not remember ever taking this standpoint. Many publications from our clinic explain that there *must first* be an *injury* of the intestinal epithelium caused by *abnormal bacterial fermentation*, before the food can itself be harmful.

On page 320 Dr. Morse says that among other reasons, we recommend the addition of buttermilk to our mixture on account of its low salt-content. This is a misunderstanding. We use buttermilk because it is a fat-free milk, with a decreased quantity of lactose.

Now a word about Dr. Morse’s results. He does not like and use eiweissmilch for a routine food, but being prepared to take advantage of the main principles of the method he employs another mixture, prepared with precipitated casein from one quart of milk, and cream containing a high percentage of fat with addition of dextrin-maltose. He does not say how much cream there was in the mixture, but from the fact that it was extremely high in fat, the quantity must have been low and we can rather calculate it. His mixture contained 2 per cent. protein, 1.8 per cent. of which was precipitated casein. This leaves only 0.2 per cent. protein from the cream as is found in about 60 gm. The content of whey is not mentioned. From this we cannot think that whey was added. Probably the mixture contained only the little quantity of whey that was found in the cream.

We believe that this very low content of whey, and therefore of salts, explains why Dr. Morse's children did not gain. A child needs not only sufficient calories of protein, fat and carbohydrate, but he needs also a *definite minimum* of salts contained in *the whey*. Give a child too little whey and he rapidly develops a salt hunger, the first symptom of which in strong children is a cessation of the gain in weight and in weak children, with nutritional disturbances, is a rapid fall in weight, even threatening death, though the caloric value of the food may be normal.

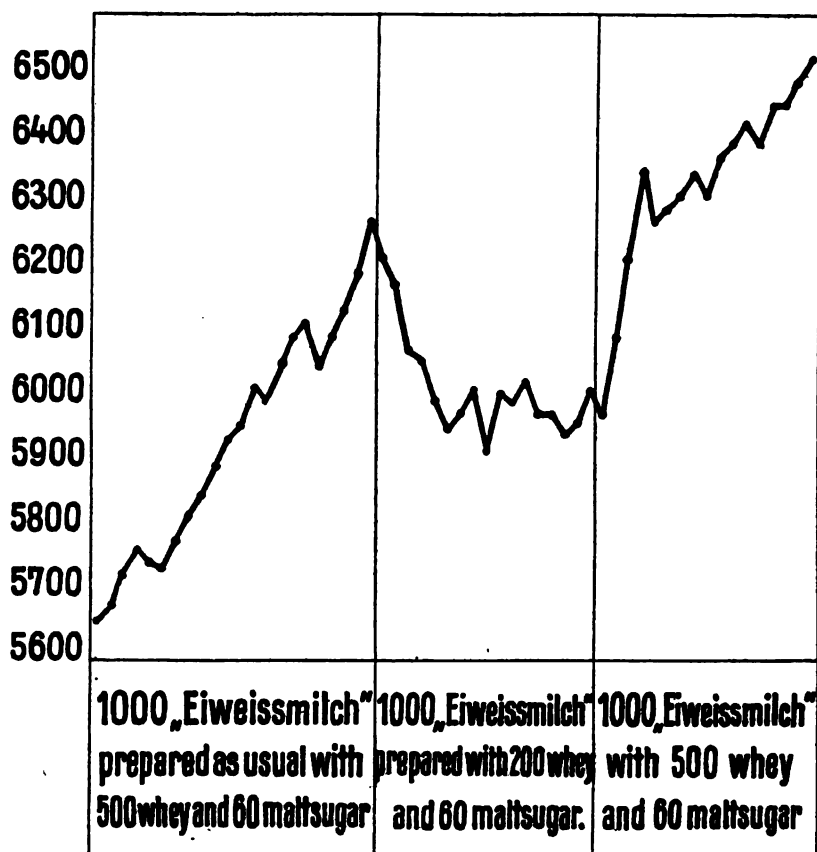


Chart showing loss of weight in grams in a healthy child on too great reduction of the quantity of whey, protein, fat and carbohydrate being sufficient.

We show, as illustration, a curve of a healthy child who got sufficient calories of protein, fat and carbohydrate, but who promptly got a loss of weight and did not thrive when the whey was too greatly reduced. From our experience, symptoms of salt-hunger appear when the whey in the mixture is reduced below 300 to 350 c.c. per liter. In the mixture used by Dr. Morse, with very low whey-content, there must have been a

marked salt-hunger in these children. Considered in this light it is self evident that no child could gain on such feeding, and we are very happy that Dr. Morse did not get worse results.

It is not just to compare this food to eiweissmilch which, as described by Dr. L. F. Meyer and myself, contains (without sugar additions) casein 3 per cent., fat 2 to 3 per cent., a little milk-sugar and almost 500 gm. of whey. We are certain that the difference in the results obtained by Dr. Morse and ourselves can be explained on this basis.

Berlin, March, 1912.

H. FINKELSTEIN.

## PROGRESS IN PEDIATRICS

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### REVIEW OF THE 1911 STUDIES IN THE NORMAL METABOLISM OF CHILDREN

J. P. SEDGWICK, M.D.  
MINNEAPOLIS

Since this subject received its discussion by Langstein and Meyer<sup>1</sup> last year, advance has been made along various lines. Unfortunately this work is not accessible to all, but Grulee's<sup>2</sup> work, now in the press, devotes considerable space to metabolism, and in a measure makes up for this deficiency in our American literature.

Ott and Scott<sup>3</sup> found that extract of the infundibulum starts the flow of milk in about one minute from the beginning of its intravenous injection, and that the excretion reaches its height in four minutes, after which it rapidly falls to normal. They found that the corpus luteum (10 grains), pineal body (5 grains) and the thymus (1 grain) increased the quantity of milk four-fold in five minutes. The ovary minus the corpus luteum had no effect. The amount of butter fat was about the same in the secretion, augmented by the thymus, corpus luteum and infundibulum.

Helbich<sup>4</sup> demonstrated that lactation can be maintained by artificial evacuation of the breast-milk without the physical stimulus of the sucking child. This can be kept up for weeks and months. He showed, moreover, that a poorly secreting breast may have its milk production increased by artificial emptying with a breast-pump. The lactation curve varies very little from that obtained in normal breast feeding.

Studies on virginal lactation made by Pfaundler<sup>5</sup> show the importance of irritation in producing a milk flow. An examination was made of the secretion of a 2-year-old calf which had not been covered or pregnant. The animal had been sucked by other calves, and Pfaundler considered it definitely proved that a fully normal, virginal animal subjected to the irritation of sucking may produce a proper and rather profuse milk

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1. Langstein and Meyer: *Infant Feeding and Metabolism* (Sedgwick Ab.), 1910, Bergman, Wiesbaden.

2. Grulee: *Infant Feeding*, 1912, Saunders, Philadelphia.

3. Ott, I., and Scott, J. C.: *The Action of Animal Extracts upon the Secretion of the Mammary Gland*, *Arch. Pediat.*, xxviii, No. 10, p. 1029.

4. Helbich, H.: *Is the Physiological Stimulus Necessary for Starting and Maintaining Lactation?* *Monatschr. f. Kinderh.*, x, No. 8, p. 391.

5. Pfaundler, M.: *Virginal Lactation*, *Ztschr. f. Kinderh.*, iii, No. 3, p. 191.



secretion. He reviews the historical cases showing similar results in the human being. He therefore considers that the usual theories concerning normal, virginal lactation require revision.

Basch<sup>6</sup> considers the activity of the breast of the new-born child to be an excellent indicator of the functional capacity of the mother's breast. He gives a very interesting résumé of the literature, as well as clinical and experimental work in supporting his position. He considers it probable that the activating bodies are carried to the fetus from the mother animal by way of the blood.

Talbot<sup>7</sup> found in every instance that the milk-supply of the mothers at the hospital was in excess of the needs of their own babies. The women were paid at the rate of 60 cents a quart for breast-milk.

Frank and Unger<sup>8</sup> give the following conclusions concerning the causes which produce the growth of the mammary gland:

1. Intra-uterine, prepuberty and puberty growth of the breasts are directly dependent on ovarian function (Tandler, Foges).

2. A cyclical change in the virgin breast occurs under the influence of the ovary.

3. Castration does not cause rapid regression of the cyclical breast hyperplasia.

4. No proof has been offered to show that the fetus or placenta directly produces growth of the breast in pregnancy.

5. Evidence points to the fact that the persistent corpus luteum of pregnancy may produce this breast growth.

6. The factors which favor or cause the persistence of the corpus luteum are unknown.

7. Certain evidence (increase of the breast produced by hydatid mole without fetus, chorio-epithelioma) makes it unlikely that the fetus is at any time the controlling factor.

8. Nature's process is more complicated than the simple chemical stimulus assumed by Starling. As yet hyperplasia of the breasts has not been experimentally produced except by parabiosis, which does not explain the stimulus. Possibly the influence of other glands of internal secretion complicates the problem.

9. Milk secretion is no index of quantitative increase in breast tissue.

10. Under physiologic conditions milk secretion sets in when the ovarian influence is removed in the new-born after birth; in the puerpera as the corpus luteum of pregnancy regresses; sometimes postoperatively

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6. Basch, K.: The Mammary Secretion of the Child as an Index of the Secretory Capability of the Mother, *München. med. Wchnschr.*, lviii, No. 43, p. 2266.

7. Talbot, Fritz B.: Two Methods of Obtaining Human Milk for Hospital Use, *Boston Med. and Surg. Jour.*, 1911, clxiv, 304.

8. Frank, Robert T., and Unger, A.: An Experimental Study of the Causes which Produce the Growth of the Mammary Gland, *Arch. Int. Med.*, 1911, vii, 812.

after castration in the virgin (if the breast has been activated by the corpus luteum of menstruation).

Knape<sup>9</sup> found no bad results in feeding children with breast-milk preserved by the addition of perhydrol. Older children are sometimes disturbed by the taste.

Grulee<sup>10</sup> concluded from clinical observations that sodium benzoate to the amount of  $2\frac{1}{2}$  to 5 grains in twenty-four hours, given to artificially fed infants ranging in age from a few weeks to almost 2 years produces no recognizable symptoms, even though these children may be suffering from gastro-intestinal disturbances of a serious nature.

Kleinschmidt<sup>11</sup> found that the proteins of cow's milk, casein, albumin and globulin may be differentiated from each other by means of anaphylactic experiments. Albumin from cow's milk and serum from cattle appear to be identical. Casein appears to be more closely allied to the globulin than to the albumin.

A. Filia,<sup>12</sup> as the result of his researches on goats, stated that uric acid and purin bases in small quantity passed through the milk; the administration of food rich in nuclein, injections of lecithin, uric acid given by mouth and by injection, slightly increased the elimination of uric acid and purin bases. He found no difference in the quantity of uric acid and purin bases eliminated by the milk in uremic or healthy women.

Barbier's<sup>13</sup> studies based on a dozen cases show a certain parallelism between the salts and the casein.

Schloss<sup>14</sup> found that the composition of the milk bears no relation to the amount produced in early lactation. Early the amount of calcium is high. This is followed later in human milk by a fairly constant amount of calcium.

According to Plauchu and Rendu<sup>15</sup> the influence of multiparity and age of the nurse, as well as the duration of the breast feeding is variable and not of great importance on the fat content of the milk. The alimentary regimen, as well as galactogogues and menstruation appear to have

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9. Knape, Walter: Breast Milk Conserved by Perhydrol, *Monatschr. f. Kinderh.*, 1911, x, No. 6, p. 281.

10. Grulee, Clifford G. and Buhlig, Walter B.: Sodium Benzoate in Artificially-Fed Children, *Arch. Pediat.*, xxviii, No. 10, p. 869.

11. Kleinschmidt, Hans: The Biological Differentiations of the Proteins of Milk, *Monatschr. f. Kinderh.*, x, No. 8, p. 402.

12. Filia, A.: Elimination of Uric Acid by the Milk, *Brit. Jour. Child. Dis.*, 1911, viii, p. 463. Seventh Congress of the Italian Pediatric Society, held at Palermo, April, 1911.

13. Barbier, M.: Session Society of Pediatrics of June 20, 1911, *Arch. de méd. d. enf.*, 1911, xiv, p. 559.

14. Schloss, Ernst: The Chemical Composition of Human Milk, *Monatschr. f. Kinderh.*, x, No. 10, p. 500.

15. Plauchu, E., and Rendu, Robert: Study of Fat in Breast Milk, *Arch. de méd. d. enf.*, 1911, xiv, p. 601.

no effect. On the contrary the more milk a nurse has the less is the butter content. The butter content is higher in the morning than in the evening. The butter content at the beginning of the nursing is higher than at the end of nursing. The smaller of two breasts gives the higher butter content. Too much fat in the milk or too little fat is thought to produce digestive troubles, especially in premature infants.

Autenrieth and Mueller<sup>16</sup> describe colorimetric methods for determination of kreatin and kreatinin based on the principle of the Folin method, and a colorimetric method for sugar, for which they claim the advantage of greater ease and rapidity.

Best<sup>17</sup> found that in the normal person foods prepared in widely different ways were well digested. He considers the importance of the cooking, in as far as the digestion is concerned, to lie mainly in its effect on the appetite and the accompanying psychic secretion and stimulation to motility.

According to Allaria<sup>18</sup> the importance of the chemical reaction of the mouth depends on its influence on the bacterial flora in the cavity, as well as its effect on the diastatic activity of the ferment. The mouth of the new-born is neutral (litmus) with frequent inclination to a slight acidity. In later infancy the contents of the mouth show various chemical reactions when examined with litmus paper. Usually blue litmus paper is turned red. The reaction is rarely neutral or alkaline. There seems to be no apparent relation between the chemical reaction of the contents of the mouth and the secretory irritation. Therefore the saliva may be considered as an almost neutral fluid. The saliva is less often and less actively acid immediately after its secretion than when it has remained in the mouth for some time. The saliva is acid to phenolphthalein.

In another communication<sup>19</sup> he states also that isosmotic food solutions such as milk, or hyposmotic food solutions, arrive in the stomach in a very definite hyposmotic condition; hyperosmotic solutions, on the contrary, go into the stomach in a less hyperosmotic condition, so that the saliva may be considered in the earliest childhood to have an important physical-chemical effect; that is, the regulation, or better, the lowering of the molecular concentration of the food solutions and therefore a decreasing of the degree of osmotic pressure (osmo-regulating or osmoderating function of the saliva).

16. Autenrieth, W., and Funk, Albert: Concerning the Colorimetric Determination of Sugar, Creatin and Creatinin in the Urine, *München. med. Wehnschr.*, vol. lviii, page 899.

17. Best, F.: Concerning the Influence of Preparation of the Food upon its Digestibility, *Deutsch. Arch. f. klin. Med.*, civ, No. 1, 94.

18. Allaria, G. B.: The Chemical Reaction of the Infant's Saliva, *Monatschr. f. Kinderh.*, x, No. 4, p. 179.

19. Allaria, G. B.: Concerning the Action of Saliva in the Beginning of Digestion in the Infant, *Jahrb. f. Kinderh.*, xxiv, No. 3, p. 252.

The arrival of the saliva food-mixture in the stomach causes the immediate secretion of gastric juice rich in hydrochloric acid and of a strong concentration, which has the effect of bringing about an osmotic equilibrium with the blood.

Salle<sup>20</sup> found it possible by means of raising the temperature beyond a certain boundary, in the case of young dogs, to bring about a disease picture characterized by great loss of weight, rise of temperature, diarrhea and vomiting. The examination of the excretory function showed a lessening of the gastric juice, a decrease of the digestive power of the ferment, a lowering of the total acidity and the content of free hydrochloric acid or even the disappearance of the latter.

Bahrtdt and Bamberg<sup>21</sup> made examinations on dogs with high duodenal fistula in which the effect of acetic acid and butyric acid was tried on the peristalsis of the stomach and intestine. The quantitative relations were especially considered. It was shown that relatively small amounts of the lower acids, amounts which gradually came into the chyme, were able to hasten the peristalsis. Moreover, they brought about a lengthened closing of the pylorus, a reflex which is to be considered as a protective arrangement for the intestine against the acid-containing food coming out of the stomach. Small amounts which, fed by mouth, brought about no increased stomach peristalsis, increased the peristalsis and brought about vomiting and diarrhea when they passed into the duodenum.

They<sup>22</sup> also found that acetic acid is the most active and the strongest among the substances examined. The higher the acid stands in the series the less active is it in causing peristalsis. It seems possible that the organic acids which are formed in the stomach normally may, in case of pathological increase of collection, be the cause of acute dyspepsia.

Huldschinsky<sup>23</sup> gives results which are to be considered in relation to normal digestion only:

1. In feeding with human milk the stomach contains only very small amounts of volatile acids. When cow's milk is fed it contains from three to six times as much.

2. The amounts of volatile fatty acids found in the stomach when cow's milk is fed corresponds with the amount of fat contained in the food. Protein and sugar, however, have no influence.

3. The formation of the volatile acids in the stomach of the normal infant can only be explained by the fermentative splitting of the glycerids

20. Salle, V.: The Effect of the Air Temperature upon the Secretory Activity of the Stomach, *Jahrb. f. Kinderh.*, xxiv, No. 6, p. 697.

21. Bahrtdt, H., and Bamberg, H.: Animal Experiments upon the Action of the Lower Fatty Acids upon Duodenal Peristalsis, *Ztschr. f. Kinderh.*, 1911, iii, 313.

22. Bahrtdt, H., and Bamberg, H.: Animal Experiments upon the Action of the Lower Fatty Acids upon Duodenal Peristalsis, *Ztschr. f. Kinderh.*, 1911, iii, 350.

23. Huldschinsky, K.: Concerning the Volatile Fatty Acids in the Stomach Content of Normal Infants, *Ztschr. f. Kinderh.*, 1911, iii, 366.

of these acids. The kind of lower fatty acid which is formed corresponds with the preformed acids in the milk fat.

Acetic acid is formed in small amounts only in the normal infant stomach. It appears possible that through a pathologic increase of the amount of cow's milk in the stomach there may arise acids which in themselves are less toxic; that is, butyric, caproic and caprylic acids, but which in greater amounts increase the peristalsis and cause acute dyspepsia.

According to Schmidt,<sup>24</sup> pieces of vegetable tissue which are left two to four hours in the incubator with a pepsin-hydrochloric acid solution and then placed in a solution of pancreatic ferments show marked softening so that a slight pressure of the finger or even a shaking of the test-tube change them into a gruel-like mass. This influence of the stomach on vegetables must be considered as a chemical action. In the past the breaking-up function of the stomach has been given too little attention in comparison with the dissolving function.

Davidsohn<sup>25</sup> states that pepsin is found in the infant stomach, but exerts no digestive action. He considers the coagulating ferment and the proteolytic ferment one.

Kleiner<sup>26</sup> found that the contents of the stomach and small intestine of normal rabbits, kept on a diet poor in easily convertible carbohydrates, when removed immediately after killing the animal, usually contain a very small but measurable amount of dextrose. A preceding nephrectomy does not increase the amounts of the dextrose in these viscera.

Sedgwick and Schlutz<sup>27</sup> found that a preliminary digestion of fat with gastric lipase increased the action of pancreatin on emulsified fat. Whether the effect shown was a summation or activation was not proved, but they concluded that the function of the gastric lipase does not end when the stomach contents pass the pylorus and are neutralized in the duodenum.

Cowie and Lyon<sup>28</sup> found that the pyloric opening and closing can be easily demonstrated in infants' stomachs. Evacuation of the stomach was delayed by experimental acidity (sustained duodenal closing reflex), as well as in experimental alkalinity (delayed pyloric opening reflex). Free acid was not found necessary for pyloric opening in the infant. In hyper-

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24. Schmidt, Adolf: Concerning the Comminuting Function of the Stomach in the Normal and Diseased Stomach, *Deutsche med. Wchnschr.*, 1911, xxxvii, No. 10, 435.

25. Davidsohn, Heinrich: Contribution to the Chemistry of the Infant Stomach, *Ztschr. f. Kinderh.*, ii, No. 5, p. 420.

26. Kleiner, Israel: The Excretion of Dextrose in the Stomach and the Small Intestine, *Jour. Exper. Med.*, 1911, xiv, 274.

27. Sedgwick, J. P., and Schlutz, F. W.: Relationship of Gastric to Pancreatic Fat Digestion in Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 243.

28. Cowie and Lyon: Further Observations of the Acid Control of the Pylorus in Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 252.

secretion in infants, protein-containing food appeared to leave the stomach more readily than water because of its binding property for acid.

Klotz<sup>29</sup> finds the acid formation in pancreatic digestion weakest with wheat. It is increased with rye, still more with barley, and to the highest degree with oats.

His results show that the bacterial content in the stool of the breast-fed child corresponds in general to that which we find in the bottle-fed child which is receiving two carbohydrates. The different forms of sugar influence the fermentative process with different intensity. Especially aggravating in effect are the starches, and among them more noticeable energetically, barley and oatmeal. It is possible to increase the number of bacteria in the feces to a maximum by a pre-arranged variation of the carbohydrates. Bacteria appear in the infant to represent from 30 to 36 per cent. of the dry fecal substance. It seems, moreover, not improbable that when an increase of the bacteria is not found when we are ministering high molecular carbohydrates, that a disturbance in the working together of the intestinal enzymes and intestinal bacteria is indicated.

Edelstein<sup>30</sup> says:

1. Dyspeptic and normal stools of breast-fed children show acetic acid as the chief constituent among the volatile fatty acids. The amount of butyric acid may be as high as 0.06 per cent. in the normal stool from the breast-fed child. In dyspeptic cases the stools may show small quantities of caprylic and formic acid.

2. The volatile fatty acids in the stomach contents of children fed with full cow's milk consists of caprylic, caproic, butyric and a little acetic acids. Caprylic and butyric acids are present in like amounts.

3. In buttermilk, according to Koppe (Vibelmilch), and in sour milk which has stood for two days, the volatile fatty acids, principally acetic acid, are present. In the sour milk up to 0.05 per cent. and in the Vibelmilch up to 0.03 per cent.; that is, acetic acid with a little butyric acid.

Bauer<sup>31</sup> confirms the work of Talbot on curds.

Brennemann<sup>32</sup> says that in all his experience he has never seen a hard curd unless a considerable amount of raw milk casein was given, and has never seen hard curds persist or occur when boiled milk, no matter in what amount, was given. He considers the difference in the action of rennin on raw and boiled milk as significant in this connection.

29. Klotz, M.: Studies on Starch Digestion, *Jahrb. f. Kinderh.*, lxxiii, 391.

30. Edelstein, F., and Csonka, F.: The Qualitative (Quantitative) Determination of Volatile Fatty Acids, *Ztschr. f. Kinderh.*, 1911, iii, 321.

31. Bauer, J.: Concerning Casein Curds in Infants' Stools, *Monatschr. f. Kinderh.*, 1911, x, No. 5, p. 239.

32. Brennemann, J.: Etiology and Nature of Hard Curds in Infants' Stools, *AM. JOUR. DIS. CHILD.*, 1911, i, 341.

While Ibrahim<sup>33</sup> confirms the findings of Wernstedt and Talbot, he also considers the casein "curds" more common in uncooked milk.

Pfaundler<sup>34</sup> calls attention to the fact that Talbot's biologic method does not show a protein body of definite chemical constitution, but only certain groups attached to the protein bodies. Therefore, strictly considered, the experiments of Uffenheimer and of Talbot and others show only the presence of such foreign radicals, not, however, the presence of casein or derivatives of the same in the infant's stool. He grants freely, however, that it is probably a casein derivative.

Stolte<sup>35</sup> considers that one common principle is fundamental in the methods of feeding which give good results, and that is the formation of soap or solid stools.

Saito<sup>36</sup> says the fat content of the feces of the infant is almost constant, either by natural or by artificial feeding; that is, it makes up about 20 per cent. of the salt constituent of the stools. Fat amounts to about 96 per cent. in the new-born child; especially in artificial feeding the fat content of the feces is usually higher and may go at times up to 40 per cent. or even more. In dyspepsia the fat content seems to be higher. Atrophic children always show a higher fat content, which becomes lower in convalescence. The feces of the new-born child, as in dyspepsia, are especially rich in oleic acid, which decreases in amount as the child grows, or in convalescence. The so-called "curds" in the feces are chiefly solid soap compounds of the fatty acids; 0.03 per cent. of the dried substance of the feces is made up of cholesterin and contains no saponifiable substances. In a rough manner the composition of the fat in the feces may be recognized by microchemical means. If a drop of concentrated sulphuric acid be put on a small piece of feces, numerous fatty acid crystals appear in the place of the soaps, and the individual fat drops are still plainer under the microscope.

Engel and Turnau<sup>37</sup> state that urines of breast-fed children react positively; that is, they show a black precipitate, while the urines of artificially fed children give a negative reaction when treated as follows: 15 or 20 drops (about 1 c.c.) of a 2 per cent. silver nitrate solution are added to 5 c.c. of urine. This is allowed to stand quietly for about ten minutes.

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33. Ibrahim, J.: Curds in Connection with the Feeding of Raw Milk, *Monatschr. f. Kinderh.*, 1911, x, No. 2, p. 55.

34. Pfaundler: Discussion of Uffenheimer's Paper Before the *Münchener Gesellschaft für Kinderheilkunde*, *Jahrb. f. Kinderh.*, lxxiv, No. 1, p. 82.

35. Stolte, Karl: Concerning the Conditions Requisite for Formation of Solid Stools of Infants, *Jahrb. f. Kinderh.*, lxxiv, No. 4, p. 367.

36. Saito, Hideo: On the Fat Content of the Feces of Infants, *Jahrb. f. Kinderh.*, lxxviii, 222.

37. St. Engel and Turnau, L.: A Reaction Given by the Urines of Breast-Fed Children, *Berl. klin. Wchnschr.*, 1911, xviii, No. 1, p. 18.

Boschan<sup>38</sup> thinks that the Engel and Turnau urine reaction does not depend on whether the child is fed with breast or cow's milk, but on the chlorid, phosphate and carbonate content of the urine.

The discoverers of the reaction state, however, that they had recognized the fact all along that the chlorin is of great importance in this silver nitrate reaction. They state that on the basis of numerous chlorin determinations in the urine of breast-fed children, they have found that this amount of silver nitrate is sufficient to oversaturate the maximum chlorin content in 5 c.c. of the urine from breast-fed children. Naturally the key to the reaction lies in these quantitative data. If the amount of silver nitrate used with the urines of the infants fed with cow's milk is increased above the saturation point, a discoloration is also produced. This, however, is different from that of the urine of breast-fed children which shows from a yellowish to a reddish brown. If there is any doubt it is advisable to compare the color with the reaction from a breast-fed normal child.

Woodyatt<sup>39</sup> and Helmholtz found the losses in "The Use of Blood Charcoal as a Clearing Agent for Urine Containing Glucose" were not constant even in the same urines, but varied widely with the weight of charcoal used, the amount of shaking and the duration of contact.

Different samples, however, acting in divergently opposite ways, make it necessary that, before any conclusions be drawn from measurements made by the Bang and Bohmannsson method, the individual sample of charcoal which is used shall be thoroughly tested in control experiments.

Amberg<sup>40</sup> and Knox consider it probable that a very appreciable part of the nitrogen contained in the urine of the normal breast-fed infant is excreted in the form of hippuric acid.

Fleischner<sup>41</sup> found that meat given twice daily to children of 6 years gives rise to a decided increase in the indicanuria and is a cause of pronounced intestinal putrefaction. This was found even more markedly the case in 3-year-old children. Meat given twice daily to 9- and 12-year-old children did not cause an increase of indicanuria. He concludes that the giving of meat more than once daily to children under 9 years of age is inadvisable.

Reuss<sup>42</sup> states that indican is often found in the urine of breast-fed children during the first weeks of life, sometimes in large quantities,

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38. Boschan, F.: The Character of the Engel-Turnau Reaction, *Berl. klin. Wchnschr.*, 1911, xviii, No. 7, p. 302.

39. Woodyatt, R. T., and Helmholtz, H. F.: The Use of Blood Charcoal as a Clearing Agent For Urine Containing Glucose, *Arch. Int. Med.*, 1911, vii, 598.

40. Amberg, Samuel, and Knox, J. H. Mason: Hippuric Acid in the Urine of Normal Breast-Fed Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 248.

41. Fleischner, Charles: The Relationship of Meat Ingestion to Indicanuria in Children, *AM. JOUR. DIS. CHILD.*, 1911, ii, 262.

42. Reuss, A.: Indicanuria in the New-Born, *Ztschr. f. Kinderh.*, iii, No. 1, p. 12.



without its being possible to demonstrate chemically any pathologic phenomenon. It is found with good nutrition and with stationary weight, with frequent bowel movements and where there is an inclination to constipation. Indicanuria is usually lacking on the first day, is rare on the second day, and is found more commonly and intensively on the third and fourth days. Moreover, during the following days its appearance is not rare.

The summary of Hamill and Blackfan's study<sup>43</sup> of the albumin in the urines of normal children is too valuable to omit:

1. There has been no relationship between the specific gravity and the form or amount of albumin.
2. The reaction has had no influence on the production of albumin.
3. Sugar, acetone and diacetic acid were never found. They may, therefore, be considered as having no bearing on the production of albumin.
4. Indican, phenol and urobilinogen when present were usually associated with albumin, but albumin was sometimes absent when they were all present, and the amount was never greater when associated with them than it was in the cases in which they were absent.
5. Crystals, when present in amounts, such as are occasionally found in normal children, are in no way responsible for the associated albumin.
6. The milk disturbances of the intestinal digestion, as shown by the examination of the stools, were not sufficient to account for the occurrence of albumin.
7. The blood-pressure was within the normal range in all cases, and therefore did not influence the albumin output.
8. The albumin elimination was the same on mixed and exclusive milk diets.
9. They found no children in whom the albumin excretion corresponded to the requirements for postural or orthostatic albuminuria, a rather surprising result in view of the frequency with which this condition is supposed to occur.
10. Thirty-two and one-half per cent. of the children showed occasional hyaline casts and cylindroids in their urines. They do not consider their "occasional presence" as indicative of a lesion of the kidneys, but rather as suggesting a temporary overtaxation of the kidneys resulting from variations in the habits of life of the individuals which are too slight to be recognized.
11. Eighty-eight and seven-tenths per cent. of the urines of these 124 children showed albumin, 27.4 per cent. showing serum-albumin alone, and in combination; and 85.4 per cent. an albuminous body precip-

43. Hamill, Samuel McClintock, and Blackfan, Kenneth D.: *AM. JOUR. DIS. CHILD.*, 1911, i, 139.

itated by acetic acid in the cold. These two albumins were nearly always present in very slight traces, occasionally in slight traces and rarely in traces.

In thirty-eight children the twenty-four-hour specimens showed nucleo-albumin in all but one, and in this case samples examined over prolonged periods of time showed nucleo-albumin frequently.

In these thirty-eight children, the percentage of serum-albumin was very much higher (42.1 per cent.) than in the total number of cases examined. They believe therefore that it is possible to demonstrate in the urine of every presumably healthy child traces of an albuminous body precipitated by acetic acid. Consequently this substance must be regarded as an exceedingly common, if not constant manifestation in the urine of children up to 14 years of age, and as of no clinical significance.

They do not believe that serum-albumin in the amounts in which it appears in these children indicates a diseased condition of the kidneys any more than does the presence of occasional hyaline casts and cylindroids, and that its etiology may be considered the same as that given for these former elements.

Simon's<sup>44</sup> statement that the urines of new-born infants on which he worked did not give creatinin reactions at the dilutions recommended by Folin does not agree with the results of Sedgwick, who found reactions of 10-250 to 10-500 dilutions to be common. All of Sedgwick's infants were at the mothers' breasts and were usually given no other fluid, which could dilute the urine. Simon found that new-born infants have a high nitrogen excretion during the first week which sinks to the normal proportions later. He found that the new-born child (during the first few days of life) excretes unsplit polypeptids up to 12 per cent.

Hadlich<sup>45</sup> finds that the amino-acid content of the urine of older children corresponds to that in adults. Diseases with fever do not generally increase it. It is, however, increased by severe enteritis. In the infant the value is generally raised, but apparently is not dependent on the condition of the child or the food or character of the stool. There is one condition especially, however, in which this does not hold, and that is alimentary intoxication. This corresponds to the views of Finkelstein in that it is in this condition that the oxidation capability of the organism is disturbed. The presence of uric acid in the urine indicates an incapacity of the organism to catabolize the amino-acids brought to it from the intestine further, to the point of ammonia, and by this means prepare them for the formation of urea.

44. Simon, S.: The Nitrogen Partition in the Urine of the New-Born, *Ztschr. f. Kinderh.*, 1911, ii, 5.

45. Hadlich, Richard, and Grosser, Paul: The Amino-Acid Content of the Urine of Children and Infants, *Jahrb. f. Kinderh.*, lxxiii, 421.

Reuss<sup>46</sup> finds that the urines of newly born children contain glycocoll as a normal constituent.

According to Birk,<sup>47</sup> in the artificially fed new-born child about one-half of the nitrogen introduced is excreted in the urine. In the naturally fed child only one-sixth to one-seventh of the nitrogen is given off. From the above a fundamental difference between the artificial and natural feeding of the new-born child is shown. It is almost like a law to be observed that the longer the period of underfeeding continues, just so much more intensive are the symptoms of exudative diathesis which develop later.

The hypodermic injection of urine in the lower animals causes the appearance of hemolytic precipitates, and complement-binding antibodies in their serum. The precipitation is always stronger with normal than with protein-containing urine. On the contrary the protein-containing urine produces more complement binding.

The apparatus designed by Lawrence<sup>48</sup> for collecting urine in female infants, for use in the Boston Floating Hospital, has been found very valuable by the reviewer. It consists of an adhesive plaster strap one-half to 2 inches wide and 4 to 6 inches long, split at one end, thus forming two tails to be directed backward and outward over the buttocks. An elliptical opening is cut through the strap and through this opening the thumb of an old rubber glove is passed and turned down on the adhesive surface of the strap. The tip of the thumb is then cut out and a test-tube inserted in the opening. The test-tube may be wrapped with adhesive, if desired, to avoid slipping. The opening in the adhesive, armed with the rubber thumb, is placed with the adhesive portion toward the body so that the opening is over the vulva. The urine is then passed directly into the test-tube.

For collecting twenty-four-hour specimens the test-tube is replaced by a piece of glass tubing which is connected by a rubber piping with a bottle placed inside the bed.

Interesting apparatus for the collection of excreta is described by Dubois,<sup>49</sup> as well as by Howland and Cook.<sup>50</sup>

The minimum, as well as the maximum, blood-pressure increases with the age of the child, according to Sahle,<sup>51</sup> and is, moreover, dependent

46. Reuss, A.: Concerning the Presence of Glycocoll in the Urine of the New-Born Infant, *Ztschr. f. Kinderh.*, iii, No. 3, p. 286.

47. Birk, W.: Contribution to Physiology of the Newborn Child, *Monatschr. f. Kinderh.*, 1911, No. 1, p. 5.

48. Lawrence, Charles H.: A Method of Collecting Urine from Female Infants, *Boston Med. and Surg. Jour.*, 1911, clxiv, 309.

49. Dubois, Eugene F.: An Apparatus for the Collection of the Excreta of Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 415.

50. Howland and Koch: A Metabolism Bed for Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 419.

51. Salle, V.: Blood-Pressure in Children, *Jahrb. f. Kinderh.*, lxxiii, 273.

within certain boundaries, on the weight and size of the child; also the height of the amplitude becomes greater with increasing age. Deviations from the average are shown in lymphatism (lower), neuropathy and nephritis (higher).

Emerich Rusz<sup>52</sup> finds the absolute values of the viscosity of the blood and refraction of the plasma to vary within wide boundaries according to the condition of the infant. The viscosity rises during the first days of life, then sinks sharply. This decrease then goes on more slowly through the whole first year. The refraction rises sharply also during the first days of life. There is then under normal conditions a decrease up to the fourth or eighth day after which it begins to rise again strongly. This rise continues then slower and slower through the whole first year of life. The day's variations of the refraction and viscosity of the blood are most marked from morning to midday. The decrease begins at mid-day and goes on until evening. The cause of the high morning value is the concentration of the blood during the eight hours of the night fast. The influence of the taking of food on the refraction and viscosity of the blood appears to differ with the condition of the child. The normal child does not seem to be affected by the food unless it causes a decrease. When the child is not progressing an increase occurs.

Miss Michael's<sup>53</sup> work confirms the blood-pressure results of Frau Wolfensohn-Kriss, as she found the pressure to increase apparently with height and weight, as well as age. She found, however, on application of Sallom's formula, thus obtaining the blood-pressure per square millimeter, that the actual blood-pressure of a 40-pound 5-year-old child and that of an 80-pound 15-year-old were practically the same.

Mills' <sup>54</sup> summary and conclusions concerning the utilization of fats and oils given subcutaneously were as follows:

"1. Olive, peanut, cocoanut, sesame, cotton-seed, lard-oils, unsalted butter-fat and lard may be given hypodermically and over a considerable period without local irritation, provided aseptic care is used, and no constitutional disturbance occurs provided precautions are used to prevent injection into the blood-stream.

2. Emulsions of these oils made with 3 to 5 per cent. of egg lecithin and water are permanent, and cause no irritation if given subcutaneously.

3. Oils and fats given subcutaneously are absorbed by means of the lymphatic system and eventually reach the thoracic duct.

52. Rusz, Emerich: Physiological Variations in the Viscosity and Refraction of the Blood of Infants, *Monatschr. f. Kinderh.*, 1911, x, No. 7, p. 36.

53. Michael, May: A Study of Blood-Pressure in Normal Children, *AM. JOUR. DIS. CHILD.*, 1911, i, 272.

54. Mills, Lloyd, H.: The Utilization of Fats and Oils Given Subcutaneously, *Arch. Int. Med.*, 1911, vii, 694.

4. Lymphatic vessels and glands in contact with and transmitting oil for any length of time become hypertrophied and are thus better able to carry oil.

5. The amount of absorption of plain oil from the subcutaneous tissues after injection during starvation is so small as to be negligible. Emulsified oils and fats injected during starvation are absorbed in amounts sufficient to furnish from one-half to two-thirds of the full calorific requirement of the animals injected.

6. Oils and fats so injected and absorbed have no more influence on the destruction of protein in starvation than has fat given alone by mouth.

7. Plain oils injected subcutaneously under conditions of low protein ingestion are little, if any, better absorbed than when similarly given during starvation. Emulsified oils injected under these conditions are absorbed quite as well as similar oils given to starving animals.

8. Plain and emulsified oils are absorbed about equally well when the animals injected are given a plentiful supply of protein in their food. This probably furnishes the large quantity of lipolytic enzymes necessary for body action on plain oil.

9. The injection of oils subjected to lipolysis causes death, which is due apparently to the production of oleic or other acids, with the possible formation of toxic quantities of soaps.

10. Oil absorbed from the tissues after subcutaneous injection is (a) burned in the body for the production of heat and energy, thus sparing the body fat; (b) retained as such within the organism; or (c) possibly converted into body fat by reconstruction in the liver, from which it may be sent for storage to the various fat depositories, after which it is drawn on as needed. Proof of this last proposition is lacking.

11. It seems likely, from comparative examination of the iodine indices of the ether extracts of visceral and adipose tissue, that the actively functioning viscera use oil and fat absorbed after subcutaneous injection for the direct performance of their functions, and that the storage of the foreign fat given in excess of the nutritive requirement takes place principally in the subcutaneous tissue, liver and lungs, to a small extent in the kidneys and spleen, while the pancreas and stomach and intestines are practically uninfluenced.

12. This demonstration that after injection under suitable conditions oils can be absorbed to an amount capable of covering so large a proportion of the calorific requirement suggests the application of such injections to the treatment of wasting diseases, to the cachectic conditions associated with imperfect metabolic processes and especially to tuberculosis, in which the intolerance to fats is almost symptomatic."

The pediatricist will at once recognize the value of a perfected method of hypodermic feeding.

Carpenter<sup>55</sup> found the energy metabolism of the new-born child expressed per unit of weight, obtained by subtracting the metabolism of the mother alone from that of mother and child together, to be two and a half times that of the mother. Expressed per unit of surface, the energy metabolism of the new-born child was not found greater than that of the nursing mother, but higher than that of a woman in complete sexual rest.

The energy quotient among the new-born fluctuates within wide range according to Samelson<sup>56</sup> so that it would probably be well in place of the former ideas, to set it at from 115 to 150 calories.

Hess<sup>57</sup> says that the energy quotient needed by premature and underweight infants averages between 115 and 170 calories when below 1,500 gm. in weight; when over 1,500 gm. the requirement is not so high — between 100 and 132 calories.

Niemann<sup>58</sup> considers the water balance the most important of his metabolism experiences. The question, "What does the difference in weight of the body on the scales mean? Is it body substances or is it water?" he believes one of greatest importance for the understanding of the condition of the child and for the condition of the metabolism processes of the infant. And this is one of the questions which we find most difficult. We have to consider the water introduced and the water formed by oxidation. Niemann believes that in weaker, normal infants, as one of his children was, water is lost with the taking on of body substance and also that when the child is brought under favorable conditions of nourishment and forced to oxidize body substance, its behavior toward the water does not change and at any rate no water is added. Under no conditions did there appear to be a tendency to putting on water in the case of simple body increase. In the case of very dry air much water was lost by the respiration. He found that with approximately the same body weight an artificially nourished child gives off considerably more carbon dioxid and water per square meter of surface than one naturally fed. On the contrary, two artificially fed children in spite of marked differences in weight gave off almost the same amount.

The daily capacity per square meter of surface was 1,347 calories. Four of his very interesting tables may be included:

55. Carpenter, Thorne M., and Murlin, John R.: The Energy Metabolism of Mother and Child Just Before and Just After Birth, *Arch. Int. Med.*, 1911, vii, 184.

56. Samelson, S.: The Contribution to the Physiology of the Feeding of Premature Infants, *Ztschr. f. Kinderh.*, 1911, ii, 31.

57. Hess, J. H.: A Study of the Pyloric Needs of Premature Infants, *AM. JOUR. DIS. CHILD.*, 1911, ii, 302.

58. Niemann, Albert: The Total Metabolism of an Artificially-Fed Infant, *Jahrb. f. Kinderh.*, 1911, lxxiv, No. 6, pp. 22, 650.

TABLE 1.—SHOWING WATER BALANCE IN AN INFANT DURING A SEVEN-DAY OBSERVATION

Water Excreted	1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day	7th Day
Through respiration ...	304.8	288.0	278.4	288.0	300.0	254.4	328.8
Through sweat .....	6.5	.....	.....	3.0	5.0	1.0	16.9
Through urine .....	500.0	470.0	490.0	445.0	510.0	460.0	405.0
Through feces .....	28.0	28.0	28.0	28.0	28.0	28.0	28.0
Total water excretion	839.3	786.0	796.4	744.0	843.0	743.4	778.7
Water given .....	693.8	693.8	693.8	668.0	668.0	689.0	745.0
Balance .....	-145.5	-92.2	-102.6	-76.0	-175.0	-54.4	-33.7

TABLE 2.—ESTIMATE OF CARBON BALANCE IN AN INFANT DURING A SIX-DAY OBSERVATION

Carbon Excretion	— Sum of Days —		24 Hr. Average for Days 1-6
	1-3	4-6	
Through respiration .....	151.3	148.0	49.9
Through urine .....	6.1	4.0	1.7
Through feces .....	8.1	8.0	2.7
Total C. excretion .....	165.5	160.1	54.3
Carbon taken in .....	224.7	168.8	68.6
Carbon balance .....	+59.2	+26.7	+14.3

TABLE 3.—NITROGEN BALANCE DURING A SIX-DAY OBSERVATION ON AN INFANT

Nitrogen Excretion	— Sum of Days —		24 Hr. Average for Days 1-6
	1-3	4-6	
In the urine .....	9.12	9.68	3.13
In the feces .....	1.20	1.20	0.40
Total Nitrogen excretion	10.32	10.88	3.53
Nitrogen taken in .....	13.25	14.19	4.57
Nitrogen balance .....	+2.93	+3.31	-1.04

Per kilogram of weight and day the following values are given:

Calorie intake (net) .....	114 cal.
Taken on .....	29 cal.
Heat formation .....	85 cal.

In this case the daily production of heat per square meter of surface amounted to 1,297 calories.

Salge<sup>59</sup> believes it important for clinical purposes that the young infant can regulate the osmotic pressure, or better, the physiologic composition of its body fluids, but imperfectly. The physiologic insufficiency of regulation, as it is seen in the young infant, gives the basis for various pathologic conditions.

59. Salge, B.: Concerning the Physical Properties of the Blood of Infants, *Ztschr. f. Kinderh.*, 1911, ii, No. 5, p. 347.

Adler and Blake's<sup>60</sup> conclusions are as follows:

1. The amount of base excreted in the urine in acidosis, while following in general the variations in the amount of ammonia, may show differences which are of importance in estimating the power of the organism to resist intoxication.

2. Whether the amount of base excreted varies with the amount of ammonia or not, it is important to determine both quantities as they represent two distinct mechanisms of defense.

Rulon and Hawk<sup>61</sup> found in their studies on water-drinking that in two of the experiments there was a pronounced increase in the output of chlorids on the days of added water intake with a return to normal during the final period. This augmented excretion of chlorids they interpreted as indicating that the large volume of water ingested during this period markedly stimulated the secretion of gastric juice. The excess hydrochloric acid, thus passed into the intestine, was reabsorbed and appeared, at least in part, in the urine as ammonium chlorid. The main bulk of the increase in the chlorid excretion they believe to have originated in this way. The flushing of the tissues and the stimulation of protein catabolism brought about by the copious water-drinking may have been contributing forces in causing the increased output of chlorid observed.

Mendelssohn<sup>62</sup> states that the power of temperature regulation is usually insufficient in very small and weak children. The capacity of regulation is gradually acquired during the first months of life and may be again lost in severe diseases such as intoxication and atrophy.

Koeppé<sup>63</sup> says that marked increases of weight above the normal may owe their occurrence to restitution or water retention. The phosphate content of the urine he found dependent on the phosphate content of the food. When he gave salt in the infant's food he noticed a rise in temperature, increase of weight and a higher amount of phosphorus pentoxid excreted in the urine. He noticed also in the infant that when it had fever and at the same time was receiving the usual amount of food, the increase of weight which depended on the water retention, was accompanied with an increased excretion of phosphorus pentoxid in the urine. In analogy with the adult, he concludes that this is dependent on a chlorin retention.

60. Adler, Herman M., and Blake, Gerald: The Retention of Alkali by the Kidney with Special Reference to Acidosis, *Arch. Int. Med.*, 1911, vii, 479.

61. Rulon, S. A., Jr., and Hawk, P. B.: Studies on Water-Drinking, *Arch. Int. Med.*, 1911, vii, p. 536.

62. Mendelssohn, A.: Observations Concerning the Surface Temperature of Infants, *Ztschr. f. Kinderh.*, iii, No. 3, p. 292.

63. Koeppé, Hans: Studies in the Mineral Metabolism, *Jahrb. f. Kinderh.*, lxxiii, 9.



Those who are further interested in the important field of salt metabolism may read Schloss' <sup>64</sup> review with profit.

Wiggers<sup>65</sup> gives a résumé of the present understanding of the physiology of the pituitary gland.

Schloss<sup>66</sup> and Crawford found the uric acid output in new-born infants both absolutely and relatively high. In the case in which the umbilical cord was ligated late they found the output of uric acid greater during the second and third days than in those cases in which the cord was ligated immediately after birth. They found the total phosphorus excretion high during the first three days and then it showed a marked diminution. They found a marked retention of the phosphorus in the new-born infant, as well as a moderate nitrogen retention during the first three days. The results show an inverse ratio between the leukocyte count and the elimination of phosphorus and uric acid during the first few days of life. They believe that the parallelism between the excretion of uric acid and phosphorus during the first three days would seem to indicate a common origin from cell nuclei.

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64. Schloss, Ernst: Progress in the Field of Mineral Metabolism of Infants During the Past Three Years, *Jahrb. f. Kinderh.*, xxiv, No. 1, p. 91.

65. Wiggers, Carl J.: The Physiology of the Pituitary Gland and the Actions of Its Extracts, *Am. Jour. Med. Sc.*, 1911, cixl, 502.

66. Schloss and Crawford: The Metabolism of Nitrogen, Phosphorus and the Purin Substances in the New-Born; With Special Reference to the Causation of the Uric Acid Infarets of the Kidney, *AM. JOUR. DIS. CHILD.*, i, 203.

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Arch. Pediat., March 29, 1912.
- Recent Developments in Pasteurization of Milk for General Market. E. H.  
Schorer.  
AM. JOUR. DIS. CHILD., April, 1912.
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Am. Jour. Public Health, Feb. 11, 1912.
- Talbot Milk Institute. A. J. Wood.  
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- Physical Examination of School Children, with Special Reference to Effect of  
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### PATHOLOGY AND BACTERIOLOGY

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- Hypertrophy of the Thymus. (Le traitement chirurgical de l'hypertrophie du  
thymus. Ses avantages, sa technique; ses résultats). E. Olivier.  
Arch. gén. de chir., February, 1912.
- Status Lymphaticus. A. R. Hall.  
St. Paul Med. Jour., April, 1912.
- Tongue with Median Raphe. (La langue scrotale chez les enfants.) J. Comby.  
Arch. de Méd. d. enf., Paris, 1912, xv.

### METABOLISM AND NUTRITION

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AM. JOUR. DIS., CHILD., April, 1912.
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Presse méd., Feb. 24, 1912.
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Deutsch. Arch. f. klin. Med., Feb. 10, 1912.

- Mineral Salts and Their Relation to Dietary of Infants and Children, B. R. Hoobler.  
Arch. Pediat., March 29, 1912.
- Desiccated Milk in Infant Feeding. (Le lait sec. dans l'alimentation des nourrissons). E. C. Aviragnet, L. Bloch-Michel and H. Dorlencourt.  
Bull. soc. pediat., Paris, 1912, xiv, No. 2.
- Great Advantages of Albumin Milk in Infant Feeding. (Zur Ernährung Neugeborener mit Eiweissmilch.) A. Benfey. (Ueber Ernährung magendarmkranker Säuglinge mit Eiweissmilch.) C. Beck.  
Jahrb. f. Kinderh., March, 1912.
- Low Percentages in Infant Feeding. R. D. Rudolf.  
Canad. Med. Assn. Jour., March, 1912.
- Medical Certification of Milk and Its Advantages in Infant Feeding. G. C. Mosher.  
Diet. and Hyg. Gaz., March, 1912.
- Milk as Food for Infants. I. A. Abt.  
Chicago Med. Rec., March, 1912.
- Prevention of Infant Mortality by Breast Feeding. W. H. Davis.  
Am. Jour. Public Health, Feb. 11, 1912.
- Use and Abuse of Carbohydrates in Infant-Feeding. C. G. Grulee.  
Jour.-Lancet, March, 1912.

#### DISEASES OF THE NEWLY-BORN

- Etiology and Treatment of So-Called Hemorrhagic Disease of New-Born. Report of Cases. O. M. Schloss and L. J. J. Commiskey.  
AM. JOUR. DIS. CHILD., April, 1912.
- Pathogenesis of Hemorrhagic Diseases of New-Born. E. A. Graham.  
Jour. Exper. Med., April, 1912.
- Subcutaneous Injection of Small Quantities of Human Blood in Spontaneous Hemorrhage of New-Born. A. W. Myers.  
Arch. Pediat., March 29, 1912.
- Familial Fatal Jaundice in Two New-Born Infants. (Zur Kasuistik des habituellen familiären Ikterus der Neugeborenen.) H. Rehn.  
Jahrb. f. Kinderh., March, 1912.
- Icteric Blood Corpuscles in Jaundice of the Newly-Born. (Ikterische Zellen im Blute bei Ikterus gravis neonatorum). P. Neukirch.  
Ztschr. f. klin. Med., Berl., March, 1912.
- Fever of New-Born. E. Boise.  
Jour. Mich. Med. Soc., March, 1912.
- Rupture of the Dura in the Newly-Born. (Les ruptures de la dure-mère crânienne chez les nouveau-nés.) L. Meyer and E. Haugh.  
Arch. men. d'obst. et de Gyn., March, 1912.
- Schultze's Swinging to Revive the Newly-Born; a Two-Edged Sword. (Zur Kritik der Schultzeschen Schwingungen als Mittel zur Wiederbelebung asphyktischer Neugeborener). M. Hirsch.  
Deutsch. med. Wchnschr., March 7, 1912.

#### ACUTE INFECTIOUS DISEASES

- Athenian Epidemic of Meningitis of 1911. C. M. Mercurius.  
Buffalo Med. Jour., March, 1912.
- Cerebrospinal Meningitis in Infant. C. W. Heitzman.  
Jour. Oklahoma Med. Assn., March, 1912.
- Dallas Epidemic of Meningitis: Laboratory Work. A. E. Thayer.  
Texas State Jour. Med., March, 1912.
- Meningitis. F. S. Cregg.  
Buffalo Med. Jour., March, 1912.

- Meningitis with *B. Coli Communis* in Cerebrospinal Fluid. G. H. Pearson.  
Lancet, London, March 16, 1912.
- Operative Treatment of Suppurative Meningitis. (Die Operation der eiterigen Meningitis.) S. Kostlivy.  
Arch. f. klin. Chir., March, 1912.
- Serous Meningitis and Blunders in its Diagnosis. (La diagnosi errata di tumore intracranico e la meningite sierosa.) A. Ceconi.  
Gaz. Osp., Milan, March 17, 1912, p. 329.
- Comparative Weight at Beginning and End of Scarlet Fever. (Om vore Skarlagensfeberpatienters Vægtforhold.) S. T. Sokrensen, and A. Levin.  
Hospitallstidende, Copenhagen, Feb. 28, 1912, p. 237.
- Gangrene of Both Calves in Scarlet Fever. (Recovery.) (Fall von symmetrischer Haut gangrän bei Scharlach.) L. Silberstein.  
Jahrb. f. Kinderh., March, 1912.
- Leukocyte Inclusions in Scarlet Fever. (Diagnostische Bewerthung von Leukocyteinschlüssen bei Scharlach.) M. Kretschmer.  
Berl. klin. Wchnschr., 1912, xlix, No. 11.
- Purpura Hemorrhagica During Convalescence from Scarlet Fever. E. C. Stevenson.  
Western Med. Rev., March, 1912.
- Diagnosis and Treatment of Diphtheria. A. B. Montgomery.  
Jour. Oklahoma Med. Assn., March, 1912.
- Diphtheria Carriers and Their Treatment. H. Page.  
Old Dominion Jour. Med. and Surg., March, 1912.
- Management of Cardiac Failure in Diphtheria. E. F. Coghlan.  
Brit. Med. Jour., March 9, 1912.
- Pulmonary Embolism as Sequel of Diphtheria. D. Stewart.  
Lancet, London, March, 1912.
- Serotherapy of Diphtheritic Paralysis. (Paralysie des deux droits externes d'origine diphtérique. Traitement par la sérothérapie. Guérison.) F. Terrien.  
Bull. Soc. Pédiat., Paris, 1912, xiv, No. 2.
- Acute Anterior Poliomyelitis in South-West Norfolk. G. F. Cross.  
Brit. Med. Jour., March, 1912.
- Analytic Study of Twenty Cases of Infantile Paralysis. A. Sophian.  
Arch. Pédiat., March 29, 1912.
- Circulation of Cerebrospinal Fluid and Its Bearing on Pathogenesis of Poliomyelitic Disease. S. P. Kramer.  
N. Y. Med. Jour., March 16, 1912.
- Interpretation of Unusual Types of Poliomyelitis. T. A. Williams.  
Am. Jour. Obst., March, 1912.
- Symptomatology of Infantile Paralysis. J. V. Manning.  
Am. Jour. Obst., March, 1912.
- Acute Glandular Fever in Children. S. V. Haas.  
AM. JOUR. DIS. CHILD., April, 1912.
- Bed Isolation of Cases of Infectious Disease. C. Rundle and A. H. G. Burton.  
Lancet, London, March 16, 1912.
- Diagnosis of Pneumonia in Infancy. O. W. Hill.  
Jour. of Tennessee Med. Assn., March, 1912.
- Dietetic and General Management of Typhoid in Children. C. G. Kerley.  
Am. Jour. Med. Sc., March, 1912.
- Differential Diagnosis of Certain Infectious Diseases. F. Thomson.  
Lancet, London, March 2, 1912.
- Erythema with Malignant Syndrome in Infectious Diseases. V. Hutinel.  
Presse méd., Paris, 1912, xx, No. 21.
- Malaria in Infant Five Months Old, Simulating von Jaksch Anemia. A. C. Henderson.  
Med. Rec., New York, March 16, 1912.

- Morbiliform Rash in a Child. J. Allan.  
Brit. Jour. Dis. Child., March, 1912.
- Periodically Recurring Parotitis; Two Cases. (Periodische Speicheldrüsenschwellungen.) C. Luders.  
Deutsch. med. Wehnschr., March, 1912.
- Relation of Chorea to Rheumatism: Analysis of 300 Cases. M. S. Fraser.  
Practitioner, March, 1912.
- Whooping-Cough. (Zur Frage der Versorgung stickhustenkranker Kinder). A. Galisch.  
Med. Klin., March, 1912.

## TUBERCULOSIS AND SYPHILIS

- Case of Pulmonary Tuberculosis with Cavity Formation in Infant Aged Three Months. E. P. Buddy.  
Jour. Missouri Med. Assn., March, 1912.
- Case of Recovery from Tuberculous Meningitis. (Heilbarkeit der tuberkulösen Hirnhautentzündung.) Hochstetter.  
Deutsch. med. Wehnschr., March, 1912.
- Conservative Treatment of Hip-Joint Disease. J. K. Young.  
Am. Jour. Orthop. Surg., February, 1912.
- Treatment of Hip-Joint Disease. E. H. Bradford.  
Am. Jour. Orthop. Surg., February, 1912.
- Treatment of Tuberculous Joint Disease with Carl Spengler's "I. K." Serum; With Report of Seven Cases. J. L. Porter and L. C. Quinn.  
Am. Jour. Orthop. Surg., February, 1912.
- Tuberculosis in Infancy and Childhood. H. Koplik.  
Bull. Johns Hopkins Hosp., April, 1912.
- Two Cases of Tuberculous Meningitis in Infants. C. A. Pfender.  
Virginia Med. Semi-Month., March 8, 1912.
- Syphilitic Affections of Bones Met with in Childhood. D. C. L. Fitz-Williams.  
Brit. Jour. Dis. Child., March, 1912.

## DIGESTIVE SYSTEM

- Appendicectomy in Five-Day Infant. (Observation de péritonite aigue probablement appendiculaire chez un enfant de cinq jours.) Canaguier and Hamel.  
Bull. Soc. Pediat., Paris, 1912, xiv, No. 2.
- Appendicitis in Children; Report of Cases. A. L. Ker.  
Western Med. Rev., March, 1912.
- The Oxyuris in Pathology of the Appendix. (Zur Frage der Bedeutung der Oxyuren bei der Wurmfortsatzentzündung der Kinder.) Rheindorf. Continued in No. 10.  
Berl. klin. Wehnschr., 1912, xlix, No. 11.
- Auto-Serum Treatment of Ascites: Cirrhosis of Liver in Infant. M. Lahiri.  
Practitioner, March, 1912.
- Cirrhosis of the Liver in the Young with Degeneration of Corpus Striatum. (L'hépatite familiale juvénile à évolution rapide avec dégénérescence du corps strié; dégénération lenticulaire progressive de Wilson.) J. Lhermitte.  
Semaine méd., Paris, 1912, xxxii, No. 11.
- Prune-Juice Vomiting as Symptom in Cyclic Vomiting in Children.  
Am. Jour. Obst., March, 1912.
- Recurrent or Periodical Vomiting. J. P. Sedgwick.  
AM. JOUR. DIS. CHILD., April, 1912.
- Cause and Treatment of Summer Diarrhea in Children. A. J. Wood.  
Australian Med. Jour., Jan. 3, 1912.
- Etiology of Infant Diarrhea. R. L. Forsyth.  
Australian Med. Jour., Jan. 13, 1912.

- Infantile Diarrhea and Its Treatment. H. A. Ellis.  
Australasian Med. Gaz., Jan. 13, 1912.
- Treatment of Summer Diarrhea. H. D. Stephens.  
Australian Med. Jour., Jan. 13, 1912.
- Stomatitis in Children. L. Kerr.  
Am. Med. February, 1912.
- Torsion of Uterine Annexa in Hernias of Nurslings. A. V. Moschcowitz.  
New York Med. Jour., April, 1912.
- Intussusception in Children. A. R. Matheny.  
Pennsylvania Med. Jour., March, 1912.
- Retrograde Enteric Intussusception. L. A. Dunn.  
Clin. Jour., Feb. 28, 1912.
- Congenital Atresia of Duodenum. (Ueber angeborenen Verschluss des Duodenums.) F. Kermauner.  
Virchow's Arch., March, 1912.
- Congenital Hypertrophic Stenosis of Pylorus in Infancy. C. P. Lapage.  
Practitioner, London. March, 1912.

### RESPIRATORY SYSTEM

- Differential Pneumograph and its Application to Children. (Der differentielle Pneumograph und seine Anwendung bei Kindern.) D. Ssokolow.  
Jahrb. f. Kinderh., March, 1912.
- Bronchopneumonia. P. P. Nesbitt.  
Jour. Oklahoma Med. Assn., March, 1912.
- Bronchoscopy for Foreign Bodies. (Bronchoskopie bei Fremdkörper.) H. v. Schrötter.  
Wien. klin. Wehnschr., March, 1912.
- Bronchoscopy for Foreign Body in Trachea or Bronchus or Both. (5 cas de corps étrangers trachéaux et bronchiques, dont deux chez le même enfant, traités par la bronchoscopie.) Guisez.  
Bull. Soc. Pediat., Paris, 1912, xiv, No. 2.
- Tracheo-Bronchial Lymphadenitis. (Les accidents de l'adénopathie trachéo-bronchique.) F. Maillet.  
Arch. de méd. d. enf., Paris, 1912, xv, No. 3.

### BLOOD AND CIRCULATORY SYSTEM

- Acute Suppurative Pericarditis in Infancy. H. Barkan and W. P. Lucas.  
Boston Med. and Surg. Jour., March 21, 1912.
- An Emergency Cannula. Transfusion in a Thirty-Six-Hour-Old Baby Suffering from Melena Neonatorum. Bertram M. Bernheim.  
Jour. Am. Med. Assn., April, 1912.
- Hemorrhagic Disease: Septicemia, Melena Neonatorum and Hepatic Cirrhosis. G. H. Whipple.  
Arch. Int. Med., March, 1912.

### OSSEOUS SYSTEM

- Adolescent Tibial Tubercle. J. Dunlop.  
Am. Jour. Orthop. Surg., February, 1912.
- Congenital Dislocation of the Hip-Joint. (La luxation congénitale de la hanche.) P. Le Damany.  
Arch. gén. de chir., February, 1912.
- Early Treatment of Scoliosis. (Scoliotique traitée depuis l'âge de six ans.) Nageotte-Wilbouchewitch.  
Bull. Soc. Pediat., Paris, 1912, xiv, No. 2.

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## A CASE OF ALLERGY TO COMMON FOODS \*

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The idiosyncrasy of certain individuals to common foods has been recognized for many years, but until recently our knowledge has depended mainly on isolated clinical observations, and the essential causes of the condition have remained obscure.

Through the courtesy of Dr. Eli Long of this city I have had the opportunity to investigate a case of pronounced idiosyncrasy to eggs, almonds and oats in a child 8 years old, the data from which furnish the basis of this communication. At the very outset I wish to acknowledge my great indebtedness to Dr. Long for the privilege of observing the case and for a number of valuable suggestions.

### I. HISTORY

*Family History.*—The maternal grandmother is affected with ichthyosis; with this exception the family history is irrelevant.

*Personal History.*—The patient, an only child, was born at term, May 10, 1904. Delivery was by low forceps and the infant was entirely normal. He was breast-fed for eighteen months and received no supplementary food until over a year old. The first teeth erupted when the patient was ten months old; he walked at the age of 18 months.

*Previous Illness.*—Beginning at the age of 3 months the patient was affected with seborrheic eczema of the face, head and limbs, which showed periods of improvement and recrudescence during the first year. At the age of 9 months he had a very severe attack of coryza. During the first 3 years of life the patient had a number of general convulsions, the first of which appeared at the age of 18 months. During this period there was evidence of a mild grade of rickets.

The patient has been subject to rather frequent attacks of inflammation of the respiratory tract. At the onset the symptoms resembled hay fever—frequent sneezing, lachrymation and coryza with a clear mucoid discharge. Attacks resembling bronchial asthma have been frequent, usually during the course of an infectious cold.

For a number of years the child has had a chronic scaly skin eruption which is most pronounced on the hands and arms but which has at various times affected the entire body. This rash is usually associated with itching. The severity and extent of involvement varies greatly from time to time. At times the rash has improved greatly and has almost disappeared, usually when he was on a restricted diet.

The patient has been free from all of the common infectious diseases.

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\*From the Laboratory of Biological Chemistry of Columbia University, at the College of Physicians and Surgeons, New York.

*Idiosyncrasy to Egg.*—The child was first given egg when 10 days old, at which time he was suffering from a slight attack of diarrhea. The white of an egg was administered in barley water and caused no symptoms whatever. The next time egg was given the patient was 14 months old, when he showed the characteristic symptoms of egg intolerance. The attempt was made to feed a soft boiled egg, of which the child took only a few tastes, cried, and refused more. Almost immediately he began to claw at his mouth and the tongue and buccal tissues swelled until they reached a size many times greater than normal. Around the mouth a distinct crop of urticarial wheals appeared. Subsequent to this experience the child refused to eat soft boiled egg.

Toward the end of his second year the action of egg on the skin was noted. The child would frequently play with empty egg shells, which always gave rise to an urticarial rash over the hands and arms.

When 22 months old egg was administered the third time. About one-eighth of an egg-white was given in milk. The child vomited immediately, the lips, tongue and inner surfaces of the cheeks became swollen and a general urticarial rash appeared.

When 2 years old, in order to determine the exact effect of egg, he was given a small quantity of partially coagulated egg-white between slices of bread. Only a very small amount was swallowed and almost immediately he began to gag and vomited profusely. The child became extremely ill. The lips, tongue and buccal tissues became enormously swollen and urticarial wheals appeared around the mouth. His face was flushed, the respirations were rapid and the mental condition dull. He soon fell into a restless sleep from which he awoke in a few moments and vomited several times. He went to sleep again and awoke after two and a half to three hours apparently well.

The next experience with egg occurred eight months later when the child ate a few small cakes in the preparation of which egg was used. Within a few moments he began to vomit and the characteristic swelling of the lips and tongue appeared. The swelling subsided within an hour.

From this time the patient was carefully guarded from all food which might contain egg, but in April, 1910, he ate a small portion of a roll the top of which was glazed with egg. The lips and tongue swelled and hives appeared around the mouth.

*Idiosyncrasy to Almonds.*—Two years ago the patient was given an almond for the first time. Very soon he complained of a queer feeling in his throat and within a few moments the characteristic swelling of the tongue, lips and mouth appeared. Other nuts had been eaten at various times with no ill effect.

*Idiosyncrasy to Oatmeal.*—During an attack of gastro-enteritis at the age of 22 months the patient was given a single feeding of oatmeal jelly from which no symptoms were observed. Oatmeal caused symptoms similar to but much milder than those due to eggs or almonds. Usually urticarial wheals appeared around the mouth and on one occasion vomiting occurred.

*Examination.*—Physical examination disclosed nothing of importance beyond the skin rash noted in the personal history. The skin of the hands and arms, and, to a lesser degree, of the trunk and lower extremities was dry and covered with fine scales. The individual scales were quite small and at most times the condition amounted to nothing more than a roughening of the skin. When the rash was at its maximum it was accompanied by itching.

The blood was examined twice with the following result: May, 1911: Hemoglobin 70 per cent. (Sahli), red cells 4,800,000, white cells 10,000. The differential count of 1,000 cells showed, polynuclear neutrophil cells, 70 per cent.; mononuclear cells, 18.6 per cent.; eosinophil cells, 10.1 per cent.; mast cells, 0.7 per cent. Oct. 7, 1911, the differential count was as follows: Polynuclear neutrophil cells, 68.1 per cent.; mononuclear cells, 19.2 per cent.; eosinophil cells, 11 per cent.; mast cells, 1 per cent. An examination of the urine at this time disclosed nothing abnormal.



## DISCUSSION

The main problems for investigation in this case are indicated by the history. The patient exhibited an idiosyncrasy toward eggs, almonds and oatmeal, foods which are entirely harmless to the normal individual. It seemed of importance to ascertain, if possible, the constituents of the foods which were responsible for the toxic symptoms. The underlying cause of the patient's allergic condition, and a means to overcome it, seemed also problems for investigation.

## II. THE REACTION

At the very outset it was necessary to devise some test other than actual feeding by which the toxic substances could be identified. Owing to the decided and at times alarming symptoms produced by the ingestion of the toxic foods, this method of investigation was considered unjustifiable.

Cutaneous inoculations on the basis of the von Pirquet tuberculin test were tried. The "borer" devised by v. Pirquet was used to produce a uniform abrasion of the skin, into which the substance to be tested was gently rubbed. The active substances produced a distinct urticarial wheal at the site of inoculation, which appeared within five to fifteen minutes after the test was made.<sup>1</sup> The intensity of the reaction varied but with the more active substances a wheal 1.5 to 3 cm. in diameter, which was elevated 1 to 5 mm. above the surrounding skin, was often produced. In stronger dilutions the active substances caused typical urticarial wheals by mere contact with the unbroken skin. The reaction was always immediate and always disappeared within one-half to one hour. After this time the skin abrasion only marked the site of inoculation.<sup>2</sup>

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1. In a case of buckwheat poisoning observed by Smith (*Arch. Int. Med.*, 1909, iii, 350), a cutaneous inoculation of this substance caused a large urticarial wheal to appear at the abraded surface. A general reaction also occurred.

2. Schmidt (*Beiträge zum Studium der cutanen Allergien*, *Arch. f. Kinderh.*, 1910, liii, 349) has made cutaneous tests with food substances on children of different ages. He used for this purpose "puro," which consists of egg white and beef extract, and a milk preparation. The positive reaction as described by him was an area of redness or a raised papule which appeared eight to twenty-four hours after the inoculation and was analogous to the reaction to tuberculin. The positive reactions bore no relation to the disease with which the children were affected but Schmidt observed that the percentage of reactions increased with age. So far as I am aware these observations have not been confirmed and out of a great number of cutaneous tests with food substances I have never observed a clearly positive reaction of this variety. In some instances the site of inoculation would show a slight redness after twelve to twenty-four hours which at times was a trifle greater perhaps than the control. But in no instance was the redness sufficiently marked to be conclusive and the formation of a distinct papule was never observed.

Itching was a frequent accompaniment but was not constant. Usually it was present with the more pronounced reactions, and always when urticarial wheals were produced by the contact of active substances with the unbroken skin.

In order that this reaction could be used as the basis of experimental work it was necessary to show that it was specific and to determine whether it could be produced by chemical or mechanical irritation alone. Pursuant of this, numerous control experiments were made.

The mechanical irritation produced by the borer alone, or by inoculation of inert substances into the abrasion, always caused a slight swelling at the abraded surface. This traumatic reaction was slightly greater, perhaps, than that present in normal persons, but was never sufficiently marked to cause any confusion. The abrasion gave rise to a perfectly circular papule about 1 to 2 mm. in diameter and identical with the slight reaction which sometimes appears immediately after a *v. Pirquet* tuberculin test.

On a number of occasions tests were made to ascertain if the patient was subject to factitious urticaria, but always with negative results. Inoculation of acids in different strengths (acetic, formic, picric, sulphuric, nitric, hydrochloric, oxalic and citric) gave no evidence of the true reaction. Alkaline substances in varying dilution (carbonates and hydroxids of sodium, potassium and ammonium) were also inactive. Numerous tests were made with solutions of salts (copper sulphate, ammonium chlorid and sulphate, sodium chlorid and citrate, uranium acetate, ferrous sulphate, etc.), all of which gave negative results. Tests were also made to determine whether the various reagents used in the preparation or extraction of the different substances to be tested might cause or inhibit the reaction. In no instance could such action be demonstrated.

These experiments showed that the cutaneous reaction was not the result of chemical or mechanical irritation. Other experiments to be described later showed that the cutaneous reaction was caused only by certain food substances and to a marked degree only by those to which the patient had exhibited a pronounced idiosyncrasy.<sup>3</sup>

The occurrence of an urticarial lesion from cutaneous inoculation of the toxic foods was directly comparable to the more striking effects produced by their ingestion—urticaria and swelling of the tissues with which they had come in contact. The swelling was strictly analogous to angioneurotic edema which is closely related to urticaria if not identical with it. The symptoms due to ingestion occurred immediately, the cuta-

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3. Control tests with preparations of eggs, almonds and oats to which the patient showed a marked reaction, were made on twenty children—from two to eight years of age—and on four adults. In no case was a reaction produced.

neous reaction was also immediate. The cutaneous reaction was considered therefore as direct evidence of the toxic nature of the substance tested.

### III. EXPERIMENTS WITH HEN'S EGGS

#### A. Egg-White

*General.*—Egg-white liquefied by cutting and diluted with distilled water produced a cutaneous reaction in the dilutions shown in Table 1.\*

TABLE 1.—EGG-WHITE DILUTED WITH DISTILLED WATER

Dilution	Reaction*	Dilution	Reaction
1 to 200 .....	—	1 to 50 .....	+
1 to 150 .....	±	1 to 20 .....	+u
1 to 100 .....	+	1 to 10 .....	+u
1 to 75 .....	+		

\* + and — indicate positive and negative reactions, respectively; ± indicates a reaction which was suggestive or at one time positive and at another negative; u indicates urticaria by contact with the unbroken skin. These symbols will be used throughout the paper.

Experiments were then undertaken to determine the nature and properties of the toxic substance (or substances) in egg-white.

1. Dialysis of egg-white through a collodion membrane against distilled water for varying periods up to seventy-two hours showed that the active substance was not diffusable. The dialysates when tested plain or after concentration to a small volume were incapable of causing a cutaneous reaction.

2. Alcohol (95 per cent.) and ether extracts and the residues obtained by complete evaporation of the solvents were inert. The residues insoluble in alcohol and ether were capable of causing a marked reaction.

3. The active substances were completely precipitated by saturation with ammonium sulphate. The filtrates freed from ammonium sulphate by dialysis, or by heating with barium carbonate, were inert. The precipitate was extremely active.

4. Egg-white was coagulated by heat and acetic acid. The filtrate was concentrated to a small volume and freed from protein by precipitation with alcohol. The protein-free filtrate was inert.

These experiments indicated that the toxic action of egg-white was due to the protein substances or to some substance intimately connected with them.

*Experiments with Proteins Isolated from Egg-White.*—Despite the vast amount of study devoted to the separation and properties of the

4. Throughout the experimental work a control test was made with each series of experiments, using distilled water or some substance previously found to be inert. All of the experiments were made at least twice; a number were repeated many times.

proteins of egg-white, the exact relationship and nature of some of the substances isolated by different workers is not clearly established.\*

It is not my intention, nor is it within the province of this paper to discuss the unity or the chemical relationship of the various proteins separated from egg-white. The attempt has been made to isolate protein substances which are apparently distinct in order to ascertain if possible the protein fraction — or fractions — responsible for the patient's symptoms.

Five proteins were separated — ovomucin, ovoglobulin, ovalbumin, ovomucoid and conalbumin. These terms refer only to the substances isolated by the methods followed. Ovalbumin was obtained in crystalline form by the method of Hopkins<sup>6</sup> and was purified by recrystallizing three times. Ovomucin was prepared by diluting egg-white with four volumes of distilled water, dissolving the precipitate in a weak solution of sodium hydroxid and reprecipitating with dilute acetic acid. This procedure was repeated four to five times, the precipitate being thoroughly washed between each precipitation.

The fractions called ovoglobulin were obtained as follows: Egg-white was precipitated by half saturation with ammonium sulphate, the precipitate mixed with a small amount of distilled water and dialysed against running water for twenty-four hours. A rather heavy precipitate in mucin-like threads and flakes settled out. This precipitate was thoroughly washed with water, pressed between layers of filter paper and dried in a current of air from an electric fan. This fraction was called *Ovoglobulin 1*.

To the filtrate was added three-eighths volume of a saturated solution of ammonium sulphate, the resulting precipitate mixed with water and

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5. Two protein fractions can be separated with a considerable degree of sharpness, ovalbumin and ovomucoid. The former can be obtained in crystalline form. The latter, owing to the fact that it is not coagulated by heat and is precipitated by alcohol without losing its solubility in water, can be obtained free from coagulable protein. There is some uncertainty concerning the relationship of ovoglobulin and ovomucin. The ovomucin of Eicholtz (*The Hydrolysis of the Albumins*, *Jour. Physiol.*, 1898, xxiii, 163) was obtained by diluting egg white with water and is considered by some to belong to the globulin fraction. Osborne and Campbell (*The Protein Constituents of Egg-White*, *Jour. Am. Chem. Soc.*, 1900, xxii, 423) used the term ovomucin for a considerable portion of the fraction precipitated from egg-white by one-half saturation with ammonium sulphate. They considered that their ovomucin was identical with that of Eicholtz. Langstein (*Ueber die gerinnbaren Stoffe des Eierklars*, *Beitr. z. chem. Phys. u. Path.*, 1902, i, 83) objects to the term ovomucin and with Corin and Berard (*Beitrag zum Studien der Albumenstoffe Eierweiss*, *Jahresb. d. Fortschr. d. Tier-Chem.*, 1888, xviii, 13) believes that there is more than one globulin in egg-white. A non-crystalline albumin with a lower coagulation temperature than the crystalline form has been described by Osborne and Campbell, and later by Langstein. This substance has been termed conalbumin.

6. Hopkins: *On the Separation of a Pure Albumin from Egg-White*, *Jour. Physiol.*, 1900, xxv, 307.

filtered. A considerable portion of the precipitate remained on the filter. The insoluble residue was washed with water and dried in the same manner as Ovoglobulin 1. This fraction was called Ovoglobulin 2.

The opalescent filtrate was dialysed against running water for twenty-four hours. No precipitation occurred. The solution was precipitated by one-third saturation with ammonium sulphate, the precipitate redissolved in water and again dialysed. This dialysed solution was used for the cutaneous test as Ovoglobulin 3.

Ovomucoid was prepared by the method of Mörner.<sup>7</sup> Liquefied egg-white was poured into boiling water acidulated with acetic acid. The mixture was heated in the presence of a sufficient quantity of acetic acid to precipitate all of the coagulable protein. The filtrate was concentrated on the water-bath and the ovomucoid precipitated by pouring into four volumes of alcohol. Purification was effected by redissolving in water and reprecipitating by alcohol several times, solution in water, dialysis for twenty-four hours, and final precipitation by alcohol.<sup>8</sup>

TABLE 2.—TESTS WITH PROTEINS ISOLATED FROM EGG-WHITE

Solution	1-20,000	1-15,000	1-10,000	1-5,000	1-1,000	1-500	1-100	1-10
Ovomucin dissolved in 0.5 per cent. sod. carb. ....	—	—	—	+	+	+	+u	+u
Ovoglobulin 1 dissolved in 0.5 per cent. sodium carbonate solution .....	—	—	—	+	+	+	+u	+u
Ovoglobulin 2 in 0.5 sodium carbonate solution .....	—	—	—	+	+	+	+u	+u
Ovoglobulin 3 .....	—	—	—	—	—	—	—	—
Ovalbumin, dissolved in distilled water .....	—	—	—	—	—	—	±	+
Ovomucoid dissolved in distilled water .....	±	+	+	+u	+u	+u	+u	+u
Conalbumin dissolved in 1 per cent. sodium carbonate solution .....	—	—	—	—	—	—	—	—
Conalbumin liquefied by artificial gastric juice .....	—	—	—	—	—	—	—	—

Conalbumin was prepared by the method of Langstein (see note 5). These protein fractions were used for the skin test with the results shown in Table 2.

These tests show that ovomucoid was the most active protein and was capable of causing a cutaneous reaction constantly in dilutions of 1 to 15,000 and frequently in dilutions as high as 1 to 20,000. Ovomucin and the fractions called Ovoglobulin 1 and 2 were next in activity. According to our present knowledge these three fractions are identical

7. Mörner: Ueber ein im Hühnereiweiss in reichlicher Menge vorkommende Muzinsubstanz, Ztschr. f. physiol. Chemie, 1894, xviii, 525.

8. I am indebted to Dr. Eddy (On the Synthesis of Some Protein Salts, Dissert. Columbia Univer., 1909) for a considerable quantity of very pure ovomucoid which he had carefully prepared for use in previous experiments.

(Osborne and Campbell, Eicholtz). Conalbumin and the fraction called Ovoglobulin 3 were incapable of causing a reaction. Ovalbumin was active only in a comparatively concentrated solution. In consideration of the fact that the first separation of ovalbumin takes place in a liquor rich in ovomucoid, and owing to the activity of ovomucoid in high dilution, it was considered possible that the reaction produced by ovalbumin was dependent on a small amount of ovomucoid mechanically incorporated in or adherent to the crystals. That such was true is indicated by the following experiment:

A concentrated solution of ovalbumin was coagulated by heat and acetic acid. The coagulum, thoroughly washed with distilled water and liquefied by the action of artificial gastric juice or dissolved in 1 per cent. sodium hydroxid solution, caused no reaction.<sup>9</sup>

The toxic action of egg-white was due, therefore, to the protein ovomucoid and to the fractions called ovomucin by Osborne and Campbell and Eicholtz.

### *B. Experiments with Egg-Yolk*<sup>10</sup>

Egg-yolk was capable of producing a cutaneous reaction in the dilutions shown in Table 3.

TABLE 3.—EFFECT EGG-YOLK DILUTED WITH DISTILLED WATER

Dilution	Reaction	Dilution	Reaction
1 to 50 .....	—	1 to 10 .....	+
1 to 20 .....	—	1 to 5 .....	+
1 to 15 .....	±		

The activity of egg-yolk was shown to be about one-tenth as great as egg-white.

Experiments demonstrated that the active constituents of egg-yolk were completely precipitated by saturation with ammonium sulphate, were insoluble in alcohol or ether and were not diffusible through collodion membranes. These properties would seem to indicate that the toxic substances belonged to the protein constituents.

9. Control experiments with the active proteins showed that the action of gastric juice for several hours or even days, was incapable of preventing the reaction. The same was true of the action of sodium hydroxid.

10. To obtain the yolks entirely free from egg-white the following procedure was used: The yolks were first washed as free as possible from the white by the method of Pennington (*A Chemical and Bacteriological Study of Fresh Eggs*, Jour. Biol. Chem., 1909, vii, 109) and then treated with 95 per cent. alcohol which served to harden the vitelline membrane and to coagulate any trace of white adherent. The alcohol was poured off and the remaining traces removed by gently blotting with filter paper. A fine pointed pipette was passed through the vitelline membrane into the center of the yolk mass. The fluid yolk was aspirated into the pipette and blown into suitable receptacles, the first and last portions in the pipette being discarded as a further precaution.

Ovovitelline was prepared by the method of Weyl,<sup>11</sup> dissolved in 0.5 per cent. solution of sodium carbonate, and tested on the patient. No reaction occurred.

#### IV. EXPERIMENTS WITH ALMONDS

*General.*—An emulsion of ground almonds produced a marked cutaneous reaction and the following experiments were undertaken to determine the nature of the toxic constituents:<sup>12</sup>

1. A substance capable of causing the reaction was diffusible through both collodion and parchment membranes. This activity of the dialysate was dependent on a protein substance which gave positive tests for proteose. About 10 gm. of finely ground almonds were dialysed through collodion against 100 c.c. of distilled water. The separate dialysates for each twenty-four hours were concentrated to a small bulk on the water-bath and used for the skin test. The results are shown in Table 4.

TABLE 4.—DIALYSIS OF AN EMULSION OF ALMONDS THROUGH COLLODION

Period of Dialysis	Cutaneous Reaction	Biuret Reaction
First 24 hours .....	+	+
Second 24 hours .....	+	+
Third 24 hours .....	+	+
Fourth 24 hours .....	+	+
Fifth 24 hours .....	+	†
Sixth 24 hours .....	*	—
Seventh 24 hours .....	—	—

\*Suggestive. †Very faint.

At the conclusion of the experiment the contents of the bag gave a positive cutaneous reaction and a strong biuret test.

2. Aqueous and 10 per cent. saline extracts of almonds were freed from protein by treatment with heat and acetic acid, concentration of the filtrate and complete precipitation of the remaining protein by alcohol. The precipitate in each instance was quite active, the protein-free filtrate was inert.

3. Saturation of an aqueous or a 10 per cent. saline extract of almonds with ammonium sulphate precipitated all of the active constituents. The filtrate when tested plain, or when freed from ammonium sulphate, was entirely inert.

4. The active substances were not soluble in alcohol (95 per cent.) or ether.

These experiments indicated that the active constituents of almonds belong to or were intimately connected with the proteins.

11. Weyl: Abderhalden's Handb. d. Biochem. Arbeitsmeth., 1910, ii, 381.

12. The almonds used in the experiments were freed from the brownish outer skins by drenching for a few moments with boiling water, since it had been found by previous experiment that these skins were incapable of causing a cutaneous reaction.

*Experiments with Proteins Isolated from Almonds.*—The globulin amandin<sup>13</sup> was extracted by treating finely ground almonds with 10 per cent. sodium chlorid solution for twenty-four hours. The extract was saturated with ammonium sulphate. The precipitate, dissolved in 10 per cent. sodium chlorid solution, was dialysed through collodion. The amandin was precipitated as a viscid, semiliquid mass which settled to the bottom of the bag. The crude amandin was washed with water, dissolved in 10 per cent. sodium chlorid and again precipitated by dialysis. The precipitate was washed thoroughly with distilled water, increasing strengths of alcohol and absolute alcohol, and then dried in a warm room.

A considerable quantity of amandin is extracted from almonds by distilled water. A small portion thus dissolved is precipitated by dialysis and is probably extracted by the neutral salts contained in the almonds. The greater portion of the amandin dissolved in an aqueous extract, however, does not separate on dialysis but is precipitated by dilute acetic acid and is probably extracted in the form of a salt. After precipitation it shows the same gross chemical and physical properties as the amandin extracted with salt solution.

A proteose was obtained from almonds by two methods: (1) A saline or aqueous extract, which gave no further precipitate on dialysis, was dialysed against increasing strengths of alcohol and precipitated by pouring into four volumes of 95 per cent. alcohol. This crude material was purified by solution in water and reprecipitation by alcohol, which procedure was repeated three times. This method gave only a very small yield of proteose, which was explained by the fact that the proteose itself was to a great extent diffusible, in consequence of which a considerable portion was lost during the dialysis against water. (2) The second method was similar to that used in preparing ovomucoid. An aqueous extract of finely ground almonds was completely precipitated by heat and acetic acid, the filtrate concentrated and precipitated by alcohol. Purification was effected in the usual manner.<sup>14</sup>

13. Osborne: Conglutin and Vitellin, *Amer. Chem. Jour.*, 1896, xviii, 609; *The Vegetable Proteins*, 1909.

14. The different preparations of the proteose gave a distinct biuret reaction in dilutions of 1 to 10,000 to 1 to 15,000. A positive reaction was given to the Liebermann, Millons, xanthoproteic, Molisch and Hopkins-Cole tests. The proteose was precipitated from an aqueous solution by picric acid, potassium ferrocyanid and acetic acid, phosphomolybdic acid, phosphotungstic acid and nitric acid. The precipitates were soluble on warming the mixtures and reappeared on cooling. Tannic acid also caused a heavy precipitate, but it was not soluble on warming. Precipitation was not effected by half saturation with sodium chlorid alone but was induced by the addition of acetic acid. Acetic acid alone caused no precipitate. Partial precipitation occurred on half saturation with ammonium sulphate. The proteose was diffusible through both collodion and parchment membranes but not completely so. Prolonged dialysis always left a non-dialysable portion which responded to the proteose tests.



The results obtained with the isolated proteins from almonds when used for the cutaneous test are shown in Table 5.

TABLE 5.—TESTS WITH THE ISOLATED PROTEINS FROM ALMONDS

Solution	1-20,000	1-15,000	1-10,000	1-5,000	1-1,000	1-100
Amandin in 10 per cent. sodium chlorid or 0.5 per cent. sodium carbonate solution* . . . . .	—	—	—	+	+	+u
Proteose in distilled water†	±	+	+	+u	+u	+u

\*Separate tests made with preparations of amandin obtained by dialysis of a saline extract, by dialysis of an aqueous extract, or by precipitation of an aqueous extract with acetic acid gave the same results.

†Preparations of the proteose obtained by direct dialysis of ground almonds, and by methods 1 and 2, gave the same results.

The proteose from almonds was therefore capable of producing a cutaneous reaction in approximately the same dilutions as ovomucoid. The diffusible nature of the proteose explains the results shown in Table 4.

The activity of amandin was less than the proteose and was comparable to the ovomucin-globulin fraction from egg-white.

#### V. EXPERIMENTS WITH OATS AND OATMEAL

*General.*—An aqueous suspension of oatmeal or finely ground oats gave a distinct cutaneous reaction which was much less marked, however, than that obtained with almonds. The general properties of the constituents of oats on which the cutaneous reaction depended were as follows:

1. Ether and alcohol (95 per cent.) extracts of oats or prepared oatmeal applied directly or after evaporation of the solvent were inert.

2. The active constituents were completely precipitated by saturation with ammonium sulphate.

3. Oatmeal and oats were dialysed through collodion against distilled water. The dialysates for each twenty-four hours were concentrated on the water-bath and used for the skin test. The dialysates for the first five days gave a positive biuret test coincident with a distinct cutaneous reaction. The dialysates for the sixth and seventh days caused no reaction when tested on the patient and were negative to the biuret test.

4. Aqueous and 10 per cent. saline extracts of oats and prepared oatmeal were freed from protein by heat and acetic acid and by precipitation of the concentrated filtrate with alcohol. The protein-free filtrate was inert.

*Experiments with the Isolated Proteins from Oats.*—The globulin avenalin was extracted and purified in the same manner as amandin from almonds. Owing to the considerable amount of starch in oats a different procedure was necessary to obtain the proteose. It was prepared by two methods: (1) Oatmeal was dialysed against distilled water until the dialysates no longer gave a positive biuret test. The dialysates were

mixed, concentrated to a small bulk on the water-bath and precipitated by 95 per cent. alcohol. Purification was effected in the usual manner. (2) The proteose was found to be soluble in 50 per cent. alcohol while but a small amount of starch was removed by this menstruum. Based on this property the following procedure was used: Oatmeal or finely ground oats were extracted with 50 per cent. alcohol for twenty-four hours. The alcohol was evaporated and the remaining aqueous extract was concentrated to a very small bulk and precipitated by 95 per cent. alcohol. The resulting precipitate was purified in the usual way by dissolving in a small amount of water and reprecipitating by alcohol.

On evaporation of the 50 per cent. alcohol extract a considerable amount of the alcohol-soluble protein, *prolamine*,<sup>15</sup> separated out. This material was dissolved in hot 65 per cent. alcohol and precipitated by allowing the alcohol to evaporate. The precipitate was again dissolved in hot alcohol and reprecipitated by pouring into a large volume of water. This precipitate was well washed with water and 95 per cent. alcohol and dried before an electric fan. The prolamine was also obtained by extracting oats with 70 per cent. alcohol and purifying by the method given above. The three proteins from oats were used for the cutaneous test with the results shown in Table 7.

TABLE 7.—TESTS WITH THE PROTEINS ISOLATED FROM OATS OR OATMEAL

Solution	1-20,000	1-15,000	1-10,000	1-5,000	1-1,000	1-500	1-100
Globulin dissolved in 10 per cent. sodium chlorid or 0.5 per cent. sodium carbonate .....	—	—	—	+	+	+	+u
Proteose obtained by alcohol extraction..	—	—	±	+	+	+u	+u
Proteose* obtained by direct dialysis .....	—	±	+	+	+u	+u	+u
Prolamine† dissolved in 0.5 per cent. sodium carbonate or 0.5 sodium hydroxid	—	—	—	—	—	—	—

\*The difference in the activity of the proteose prepared by alcohol extraction and that prepared by direct dialysis is probably due to the fact that the latter was in a purer form. It was found that the former contained some starch, while the latter was almost starch free.

†Uniform results were obtained with several different preparations of this protein.

The experiments with oats have practically the same significance as those with almonds. The active substances were closely associated or identical with the proteins. An active substance (proteose) was diffusible. The prolamine from oats was incapable of causing a cutaneous

15. Osborne: The Proteids or Albuminoids of the Oat Kernel, Amer. Jour. Chem., 1891, xiii, 327; The Vegetable Proteins, 1909.

reaction, the globulin was active in approximately the same dilutions as the globulin from almonds. The proteose from oats was slightly less active than the proteose from almonds.

#### VI. TESTS WITH OTHER FOODS

Various foods were used for the skin test as control experiments and also to determine whether certain substances biologically related to the toxic foods were capable of causing a reaction. The results are given in the accompanying tables.

TABLE 8.—RESULTS OF SKIN TESTS WITH VARIOUS FOODS, BLOOD SERUMS, ETC.

Food substances related to almonds (Rosaceae)	Tests with various nuts	Miscellaneous food substances
Peach kernel . . . . . +	Brazil nut . . . . . —	Peas . . . . . —
Prune kernel . . . . . +	Pecan . . . . . —	Beans . . . . . —
Plum kernel . . . . . +	English walnut . . . . . —	Cabbage . . . . . —
Strawberry seed . . . . . +	Black walnut . . . . . —	Sweet potato . . . . . —
Apple seed . . . . . +	Chestnut . . . . . —	Irish potato . . . . . —
Pear seed . . . . . +	Butternut . . . . . —	Parsnips . . . . . —
Cherry seed . . . . . +	Hazelnut . . . . . —	Carrots . . . . . —
	Peanut . . . . . —	Cauliflower . . . . . —
	Skin tests with chicken and related blood sera	Tea . . . . . —
Other fruit seed	Chicken—	Coffee . . . . . —
Grape . . . . . —	Hen . . . . . +	Milk . . . . . —
Orange . . . . . —	Rooster . . . . . +	Sugar . . . . . —
	Duck . . . . . +	Bananas . . . . . +
	Turkey . . . . . +	Tests with proteins chemically related to the active proteins from eggs, almonds and oats
	Goose . . . . . +	Witte's peptone (proteose) . . . . . —
Food substances related to oats	Tests with miscellaneous blood sera	Bence Jones protein* . . . . . —
Rice . . . . . +	Lamb . . . . . —	Nucleoalbumin . . . . . —
Barley . . . . . +	Horse . . . . . —	Salivary mucin . . . . . —
Corn . . . . . —	Calf . . . . . —	Ovomucoid from shad roe† . . . . . —
Wheat . . . . . —	Pig . . . . . —	Tendomucoid‡ . . . . . —
Rye . . . . . +	Fish (whole blood) . . . . . —	

\*Obtained through the courtesy of Dr. J. Rosenbloom of this Laboratory. "A Contribution to the Study of the Nature and Origin of the Bence-Jones Protein." Dissertation, Columbia University, 1909.

†This preparation was kindly supplied by Dr. Eddy and was prepared during previous experimental work, "On the Synthesis of Some Protein Salts." Dissertation, Columbia University, 1909.

‡One of the many preparations Prof. Gies has used in previous researches on glycoproteins.

These experiments show that the cutaneous reaction was only relatively specific and was caused by substances biologically related to eggs, almonds and oats. The reaction was produced not only by the blood-serum of the chicken, but also by that of the turkey, goose and duck. The serums of creatures not biologically related (sheep, horse, pig and cow) caused no reaction. Certain plant substances which belong to the

same family, as almonds, also caused the reaction. The results with foods related to oats were somewhat though not quite similar. Rice, barley and rye were capable of producing a mild reaction, but wheat and corn were apparently inert. On the other hand seeds of fruits and various vegetable foods which were not related to almonds or oats were incapable of causing a reaction. Bananas, however, furnish a striking exception for they caused a pronounced skin reaction. It is interesting to note that although rice, barley, rye and bananas were capable of causing a skin reaction, yet they had been eaten at various times without the production of definite symptoms.

#### VII. EXPERIMENTS WITH THE ACTIVE SUBSTANCES

It was demonstrated by experiments previously described that the cutaneous reaction was caused by various proteins from eggs, almonds and oats. These results indicate that the reaction was dependent on the protein substances themselves or on some substance intimately connected with them. It seemed desirable, therefore, to ascertain if possible whether the reaction was caused by the proteins themselves, or whether it was due perhaps to some contaminating substance which, though distinct from the proteins, was inseparable by the ordinary methods of preparation.

*Effect of Heat.*—In the preparation of the proteoses from almonds and oats and of ovomucoid, a considerable degree of heat was used which had no apparent influence on the cutaneous reaction. To determine definitely if heat had any power of impairing the reaction, the following experiments were made: Solutions of 1-to-10,000 ovomucoid and the proteoses were placed in test-tubes and immersed in boiling water for three hours. Any loss by evaporation was made up and the solutions tested on the patient, using a part of the original (unheated) solution as a control. There was no perceptible difference in the reactions.

*Dialysis.*—Ovomucoid and the globulins from oats and almonds did not pass through a collodion membrane and the dialysates, though concentrated to a very small bulk, did not cause a cutaneous reaction. The proteoses from almonds and oats were to a great extent diffusible through collodion and parchment membranes and the patient reacted to the dialysates as long as they gave a positive biuret test. When the dialysates no longer contained protein, no cutaneous reaction was given. At this time, however, the contents of the bag still contained a non-diffusible residue which responded to the proteose tests and was capable of causing a cutaneous reaction.

*Fractional Precipitation with Ammonium Sulphate.*—Aqueous solutions of ovomucoid and the proteoses from almonds and oats were precipitated by the graduated addition of ammonium sulphate. The demarcation of the different precipitates was not sharp, but from four to six fractions were obtained for each protein. Each fraction caused a cutaneous reac-

tion in dilutions of from 1 to 14,000 to 1 to 8,000.<sup>16</sup> The final filtrates which had been saturated with ammonium sulphate caused no reaction.

*Precipitation with the Alkaloidal Reagents.*—Aqueous solutions of ovomucoid and the proteose from almonds were precipitated by phosphotungstic and phosphomolybdic acids, by potassiomeric iodid, potassium ferrocyanid and acetic acid and tannic acid. The mixtures were filtered and the filtrates used for the skin test. In no instance was a cutaneous reaction produced.

TABLE 9.—THE EFFECT OF TRYPTIC DIGESTION UPON THE ACTIVITY OF OVOMUCOID AND THE GLOBULINS AND PROTEOSES FROM ALMONDS AND OATS

Duration of Digestion, Days	Ovo- mucoid		Globulin Oats		Proteose Oats		Globulin Almonds		Proteose Almonds	
	Cutaneous Reaction	Biuret Reaction	Cutaneous Reaction	Biuret Reaction	Cutaneous Reaction	Biuret Reaction	Cutaneous Reaction	Biuret Reaction	Cutaneous Reaction	Biuret Reaction
7 .....	+	+	+	+	+	+	+	+	+	+
11 .....	+	+	+	+	++	+	+	+	+	+
13 .....	+	+	+	+	—	+	+	+	++	+
15 .....	+	+	+	+	..	..	+	+	—	+
19 .....	+	+	—	+	..	..	++	+	—	+
24 .....	+	+	—	+	..	..	—	+	..	—
46 .....	+	+	—	+	..	..	—	+	..	..
56 .....	+	+	—	+	..	..	..	..	..	..
74 .....	—	+	..	..	..	..	..	..	..	..
80 .....	—	+	..	..	..	..	..	..	..	..

\*Faint.

*Adsorptive Properties.*—If the active substances were chemically distinct from, but mechanically adherent to, the proteins, it was considered possible that this adsorptive tendency might be manifested by other proteins. In the effort to ascertain whether this was true, the following experiments were made:

Ten c.c. of horse's blood-serum was mixed with an equal volume of 1 to 10,000 solutions of ovomucoid and almond proteoses. The mixtures were acidulated with acetic acid and coagulated by heat. The well-washed coagulums, plain, or liquefied by artificial gastric juice, caused no reaction on the patient. The experiments were repeated using sheep instead of horse blood-serum. The results were also negative.

*Effect of Tryptic Digestion.*—Ovomucoid and the globulins and proteoses from almonds and oats were digested by means of an active pancreatic extract. The proteins were dissolved in 0.5 per cent. sodium carbonate solution in dilutions of 1 to 500 and 1 to 1,000 and digested at 37 C. Toluol was used as a preservative. From time to time portions of the material were removed and used for the skin test, the results of which are given in Table 9.

16. All of these precipitates contained ammonium sulphate, which accounts for the fact that they gave the reaction only in more concentrated solution than the pure proteins.

These experiments showed that the activity of the proteins was destroyed by tryptic digestion and that the cutaneous reaction disappeared before the proteins were completely hydrolysed. It seemed, therefore, that the cutaneous reaction was dependent on some grouping of the protein molecule higher than the peptones. In order to determine this point with greater accuracy the globulins from almonds and ovomucoid were subjected to tryptic digestion for fifteen days, at which time the mixtures were capable of producing a marked reaction. No precipitate was produced by neutralization with hydrochloric acid. The substances precipitated by saturation with ammonium sulphate produced a marked skin reaction; the filtrate gave a distinct biuret reaction but produced no effect when tested on the patient.<sup>17</sup>

These experiments demonstrate that the substances responsible for the cutaneous reaction partook of the general properties of the proteins and that it was impossible to obtain an active substance distinct from the proteins. On gradual hydrolysis of the active proteins with trypsin the cutaneous reaction disappeared before the biuret reaction. So far as one can judge from these experiments it seems probable that the cutaneous reaction was dependent on some definite grouping in the protein molecules.

#### VIII. THE NATURE OF THE PATIENT'S HYPERSUSCEPTIBILITY

The next problem of importance concerned the nature of the patient's idiosyncrasy. Obviously his hypersusceptibility to the food proteins was due to one of two causes. Either he lacked some protective substance which is present in normal individuals, or he was sensitized in some way to the food proteins.

A number of experiments were undertaken in the effort to demonstrate the presence of a protective substance in normal individuals. Four specimens of human blood (citrate) and human blood-serum were mixed with different dilutions of the active proteins and tested on the patient immediately or after incubation at 37 C. In no instance did these solutions give a less active cutaneous reaction than the controls which were of the same dilution but did not contain blood or serum. Moreover, the minimum dilution of the active substances necessary to induce the cutaneous reaction was entirely independent of the presence of human blood or serum in the solutions.<sup>18</sup>

17. Results obtained by hydrolysis with 25 per cent. sulphuric acid were practically identical with those obtained by tryptic digestion.

18. The attempt was also made to determine whether the patient's blood contained some substance which by its action on or combination with the active proteins was capable of producing urticaria. Mixtures of the patient's blood and blood serum in different proportions with varying dilutions of ovomucoid and the proteoses from almonds and oats were tested on normal individuals. The tests were made immediately after mixing and also after varying periods of incubation at 37 C. In no instance was urticaria produced.

These experiments being entirely negative, the attempt was made to sensitize passively guinea-pigs to egg my means of the patient's blood-serum. The results of the experiments are shown in the following protocols:

1. A 260 gm. guinea-pig was given 6 c.c. of partially inactivated<sup>19</sup> blood-serum from the patient by intraperitoneal injection. Twenty-five hours later 150 mg. of ovomucoid by intraperitoneal injection. The development of symptoms was as follows: 15 minutes after injection, coat roughened, animal uneasy. Twenty minutes: cough, stridor, recession of sides on inspiration, slight diarrhea. Twenty-five minutes: dyspnea increasing, tendency to lie on side. Forty-five minutes: body limp, respirations labored. Apnea and death 82 minutes after injection. Autopsy: Lungs whitish and enormously distended leaving but a small triangular area of the heart uncovered, petechial hemorrhages in intestinal wall. Heart continued to beat over 10 minutes after the thorax was opened.

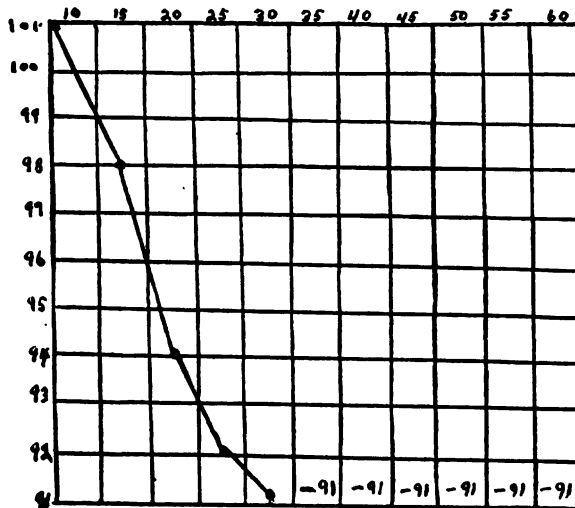


Chart 1.—Temperature Curve of Guinea-Pig 1. Figures at the left indicate the temperature F. The thermometer was not graduated below 91 F. The figures at the top indicate minutes after the injection.

2. Weight 290 gm.; 6 c.c. of partially inactivated blood serum from the patient by intraperitoneal injection; twenty-nine hours later 150 mg. of ovomu-

19. In the first experiments the attempt was made to inject the blood-serum in active form. The active serum was extremely toxic for guinea pigs, 3 c.c. being sufficient to cause the death of a 250 gm. pig within eight to ten hours. The serum was then partially inactivated by heating at 53 to 54 degrees C. for sixteen minutes. After this treatment the serum still caused the animals to become slightly ill (roughening of coat, lachrymation, slight dyspnea), but they recovered completely within a few hours. The toxic action of normal blood-sera has been studied by Uhlenhuth, Pfeiffer (*Ueber die nekrotisierende Wirkung normaler Seren*, *Ztschr. f. Hyg. u. Infektionskr.*, 1905, li, 183; *ibid*, *Wien. klin. Wchnschr.*, 1909, xviii, 465; *Das Problem der eiweiss Anaphylaxie*, etc., 1910) and others and is considered due to a definite antibody, probably hemolytic. According to Pfeiffer the symptoms due to the injection of toxic foreign sera are practically identical with those of anaphylaxis.

coid (in normal saline) by intraperitoneal injection. Fifteen minutes: animal uneasy, roughening of coat; 25 minutes: Dyspnea, recession of sides on inspiration, cough; 45 minutes: body limp, lying on side; respirations slowed and labored; began to improve about an hour after the injection and had recovered completely in about five hours.

*Controls.*—Four guinea-pigs about 250 gm. in weight each, were given 6 c.c. of normal human serum (partially inactivated) by intraperitoneal injection. Twenty-four hours later three were given 150 mg. of ovomucoid by intraperitoneal injection. Beyond a fall of temperature of 1 to 3 degrees F. they developed no symptoms. The remaining animal was given 2 c.c. of inactivated horse serum by intraperitoneal injection. No symptoms developed.

These experiments demonstrate that the patient's blood-serum contained some substance which was capable of sensitizing guinea-pigs to ovomucoid. It seems justifiable to assume therefore that the allergic condition of the patient — to egg at least — was due to protein sensitization or anaphylaxis.<sup>20</sup>

#### IX. IMMUNIZATION. THE RELATIONSHIP OF THE PATIENT'S ALLERGY TO EGGS, ALMONDS AND OATS

The next, and the most important problem from a practical standpoint, was that of immunization.<sup>21</sup> The patient's marked idiosyncrasy to egg was, to say the least, a great inconvenience. A vast amount of care was required in the preparation and supervision of his food and a number of palatable and nutritious food preparations were excluded from his dietary. With the problem of immunization was also connected several points of scientific interest.

The history of the patient indicates that his idiosyncrasy to egg was not congenital but was acquired at some time when he was between the ages of 10 days and 14 months. It seems possible that sensitization occurred at the time egg was first administered. In reference to oatmeal the history is similar. The first administration of oatmeal when the patient was 22 months old caused no symptoms; subsequently the ingestion of oatmeal caused characteristic urticarial lesions.

On the other hand, so far as can be ascertained from the history, toxic symptoms occurred the first time almonds were eaten. To explain his

20. These experiments have a close analogy to those of Bruck (*Experimental Beiträge zur Aetiologie und Pathogenese der Urticaria*, Arch. f. Dermat. u. Syph., 1909, xcvi, 241). The patient was susceptible to urticaria from the ingestion of pork. Bruck was able to sensitize guinea-pigs to pig's serum by means of injections of the blood-serum of the patient. The experiments were admirably controlled and were conclusive in every way.

21. The only recorded instance of immunization in a case of idiosyncrasy to egg that I have been able to find is that of Scofield (*A Case of Egg Poisoning*, Lancet, London, 1908, i, 716) whose patient suffered from disturbances practically identical with those of my own patient. Scofield began by administering minute quantities of egg in pills (1-10.000 part of a raw egg), gradually increased the dose and later gave foods containing small amounts of egg. By this means the patient was cured of the idiosyncrasy.



hypersusceptibility to almonds three possibilities were suggested: (1) The condition may have been congenital; (2) the patient may have been sensitized by eating a small amount of almonds, which circumstance escaped the observation or memory of the parents, though this seems most unlikely; (3) the sensitization to eggs or oats may have in some way rendered him hypersusceptible to almonds. There would be no means of ascertaining whether the first or second hypothesis was correct. From the results of immunization, however, evidence could be obtained which would serve to show the correctness of the third hypothesis.

It seemed preferable therefore to use a single protein for immunization rather than any one or all of the three foods, as by this means it could be ascertained whether the patient's hypersusceptibility to the different proteins and foods was in any way related. If, for example, immunization to one protein from the egg also induced immunity to the other active

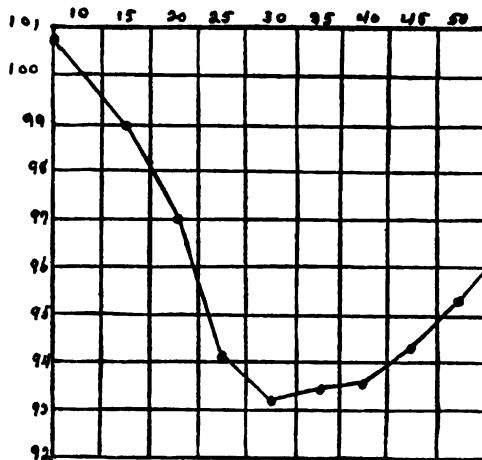


Chart 2.—Temperature curve Guinea-Pig 2. The figures at the left indicate the temperature F. The figures at the top indicate the numbers of minutes after the injection.

protein from this source, it would show that the patient was not sensitized to the distinct proteins but to some constituent group common to both. If immunity to almonds and oats also occurred, proof would be ample that the patient's allergic condition was specific neither for the protein molecule as a whole nor for the proteins of a single source, but to some group common to the active proteins of all three foods.

On the other hand, if immunity was induced only to the protein administered, or to proteins of the same source, a separate sensitization to each protein, or to each food, must be assumed.

Ovomucoid was selected as the protein for immunization, as it was one of the most active and could be prepared easily and in a state of comparative purity.

Treatment was begun Oct. 28, 1911, by the administration of 2 mg. of ovomucoid in capsules three times a day. The dose was increased at first gradually and then more rapidly. At first the quantity was increased at the rate of 2 mg. a day and on November 19 the daily increase was raised to 6 mg. Subsequently the daily increase was as follows: from November 26 to December 5, 12 mg.; from December 5 to December 14, 24 mg.; from December 14 to December 23, 48 mg.; from December 23 to January 1, 78 mg.; from January 1 to January 14, 190 mg.; from January 14, 380 mg. Toward the end of immunization the patient was taking over 7 gm. of ovomucoid a day.

The progress of immunization was determined by means of the cutaneous reaction. About the first of December the reaction began to decrease and was induced only by comparatively strong dilutions of ovomucoid, 1 to 500 and stronger. On January 8 the reaction had decreased greatly and on January 11 a small amount of egg-white was touched to the patient's lips. No disturbance occurred and on January 12 the patient ate about one-sixth of an egg with no ill effect.

From this time foods containing egg, and also soft boiled or raw eggs, were fed each day. The foods containing egg caused no symptoms. At first the patient complained that soft boiled egg caused his mouth to sting or itch but these sensations were accompanied by no objective disturbances and later disappeared. During the immunization the patient was in comparatively good health and presented no symptoms referable to the administration of the ovomucoid. The larger doses of ovomucoid, however, produced a fall of temperature which was most pronounced after a marked increase in the dose and at times amounted to 1.8 F. This fall of temperature would gradually become less pronounced. When the dose was again greatly increased the fall of temperature would recur.

The cutaneous reaction to egg and the proteins from egg has entirely disappeared. The proteose from oats causes no reaction in dilutions as great as 1 to 50 and oatmeal has been eaten a great number of times with no resulting symptoms. A distinct cutaneous reaction is still given to a 1 to 500 dilution of almond proteose. A 1 to 100 dilution is capable of causing urticaria by contact with the unbroken skin. Dilutions weaker than 1 to 1,000, however, cause no cutaneous reaction. The decrease in the patient's reaction to this substance is shown by comparison with the results in Table 5. Almonds have been eaten several times; in most instances the patient complained of itching of the tongue or throat, but usually nothing was visible on examination. On two occasions, however, urticarial wheals appeared on the inner surface of the lower lip. This disturbance appeared to be less than that which occurred previous to immunization. A differential blood count on February 7 was as

follows: polynuclear cells, 64 per cent.; mononuclear cells, 27.3 per cent.; eosinophils, 8.1 per cent.; mast cells, 0.2 per cent.

The above experiments showed that the administration of ovomucoid by mouth completely immunized the patient to egg. It is therefore apparent that he was not sensitized to the distinct proteins of the egg but to some constituent group common to the toxic proteins. At the same time the patient became entirely immune to oatmeal and less sensitive, though not immune, to almonds. Judging from these results it would seem that the patient's allergic condition to the three dissimilar foods was in some way related. Our present knowledge of the subject is too meager, however, to interpret these results as proving that the original sensitization to egg or oats also sensitized the patient to almonds. Moreover, the results from a single case are insufficient data on which to base this view, which is not in accord with the current ideas of the specificity of anaphylaxis.<sup>22</sup> Another possibility which must be considered is that the sensitization to egg and oats, although not the direct cause of the patient's idiosyncrasy to almonds, may have served in some way as a predisposing cause.

#### X. SUMMARY

In a boy now 8 years old marked urticarial lesions were caused by the ingestion of eggs, almonds and oatmeal. The idiosyncrasy to egg was not congenital but was acquired at some time between the ages of 10 days and 14 months. Symptoms due to the ingestion of oats appeared some time after the child had first eaten oatmeal when he was 22 months old. As far as can be ascertained, the idiosyncrasy to almonds was manifested the first time this food was eaten.

It was found that cutaneous inoculation of these and certain related food substances produced an urticarial wheal at the site of inoculation. The cutaneous reaction was produced only by the protein constituents of eggs, almonds and oats. Different proteins from the same source varied in activity, some being incapable of causing a reaction. Some of the active proteins caused urticaria by mere contact with the unbroken skin.

It was possible passively to sensitize guinea-pigs to ovomucoid (one of the active proteins from eggs) by intraperitoneal injections of the patient's blood-serum.

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22. Our present knowledge of anaphylaxis, however, is derived almost entirely from animal experiments and there is no proof that the specificity of the phenomenon is the same for all species. It is quite possible that the reaction in man is not specific, and other cases of food allergy which are under observation at the present time support this view. On the other hand, it is also possible that there is some fundamental condition present in certain individuals which may predispose to sensitization by food substances. If this were true the individual may be sensitized separately to each food to which he reacts and the non-specificity of anaphylaxis in the human being may be only apparent and not real.

By feeding ovomucoid in gradually increasing doses the patient became immune to egg. At the same time immunity to oatmeal and an apparently decreased susceptibility to almonds occurred.

I wish to acknowledge my deep indebtedness to Professor Gies for his kindness in placing the facilities of his laboratory at my disposal, and to him and his associates for much assistance. It is a pleasant duty to express my thanks to the parents of the patient not only for their patience and cooperation during ten months of tedious experimentation, but also for a number of valuable observations.

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## THE WASSERMANN REACTION IN INFANTS AND CHILDREN: A CLINICAL STUDY\*

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The diagnosis of early congenital syphilis as a rule is not difficult. The diagnosis of the same disease in later childhood is often a matter of great difficulty. Careful inquiry into the history, both family and personal, may throw no light on the case, and the characteristic signs which would enable one to make a diagnosis may be slight, or entirely absent; yet, later, perhaps at the age of puberty, such signs do arise and the diagnosis is evident. Undoubtedly such cases are syphilitic from the onset, but run a "latent" course, perhaps for several years, and then under certain conditions break out in a more pronounced form.

The diagnosis being thus at times difficult, any measures leading to ease and certainty of detection are eagerly welcomed. Studies of recent years have given us three such measures: the detection of the *Spirochaeta pallida* in the secretions or tissues of the body, inoculation experiments on monkeys or rabbits, the serum reaction of Wassermann. While the clinical diagnosis will continue to be the most important method in the future, as it has been in the past, these other recent methods will be of great value especially in obscure, latent cases. Of these methods the serum reaction is the most widely used and of the greatest practical value. This method depends on the complement-uniting reaction first described by Bordet and Gengou in 1901. In 1905 Wassermann applied this reaction to the diagnosis of syphilis.

"The reaction depends on the fact that serum from a positive syphilitic patient contains certain reaction bodies or antibodies which, in the presence of a known antigen from the liver of a syphilitic fetus, combines with the complement. The complement being bound in this first step, does not enter into combination with the hemolytic system, which is the indicator in the reaction, and therefore hemolysis is prevented, or inhibition of hemolysis occurs, giving a positive reaction. If the serum of a normal person is brought into combination with a known syphilitic antigen, derived in the same way as above, there is no union with the complement, which consequently is left free to unite with the hemolytic system, the indicator again, and hemolysis does occur, giving a negative reaction."

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\*From the Children's Memorial Hospital.

\*Read before the New England Pediatric Society, March 30, 1912.

In most of the tests made in this series, the Noguchi modification of the Wassermann method has been used. It is not the intention of this paper to enter into a discussion of the relative merits of Wassermann's original method and Noguchi's modification thereof. The evidence seems conclusive, to a clinician at least, that the Noguchi method is fully as reliable as, and perhaps more sensitive than, the Wassermann technic, and yet in the hands of an expert is not too sensitive, i. e., does not give positive results in non-syphilitic cases (Kaliski). It furthermore has the advantage of requiring less blood, a factor of no little importance in carrying out the technic in small children.

#### TECHNIC

The various steps are as follows: The blood may be obtained from either a vein or, preferably, from a finger or the great toe; only about 1 c.c. is required; to obtain this a finger or the great toe is punctured with a Hagedorn needle, the part massaged toward the puncture and the blood collected in a Wright capsule (Fig. 1). "The straight empty end of the tube is now sealed with a flame, cooled, shaken to drive the blood from the bent end to the straight sealed end, and the bent end is then sealed in the flame. Care must be taken not to apply the heat to the blood itself. After sealing, the tube may be mailed to the serologist for examination. Wright's capsules may be made by drawing out ordinary thin glass tubing in the flame of an alcohol lamp or Bunsen burner.

"The blood clot and the serum separate in a few hours at room temperature. If the test is not made within two or three days, the serum should be drawn off with a capillary pipet; otherwise, if left in contact with the clot, it will become tinged with the hemoglobin and this will somewhat interfere with the accurate reading of the test"<sup>1</sup> (Fig. 2).

The spinal fluid may be used for the test in cases in which a lumbar puncture is done for either diagnostic or therapeutic purposes, or in certain cases of emaciated, atrophic infants where it seems impossible to obtain enough blood and where a test is imperative; in the latter class of patients a lumbar puncture may be done especially for this purpose. It must be borne in mind, however, that in a small proportion of cases, the spinal fluid will give a negative reaction, when the blood gives a positive one.

#### DIAGNOSTIC VALUE OF SERUM TEST

The Wassermann test has now been applied to thousands of cases of undoubted syphilis in adults, has been found present in from 60 to 100 per cent. of the cases, according to the stage of the disease, and is universally accepted as of great diagnostic value. The test has also been applied

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1. Noguchi: *Serum Diagnosis of Syphilis*, ed. 2, 1911, p. 54. Lippincott Co., Phila.

to syphilitic infants and children, though in smaller numbers, and among them also is regarded of great diagnostic significance. Various observers — Mulzer and Michaelis, Bauer, Halberstaedter, Muller and Reiche, Reinhart, Stroscher and others — applying the test to cases of manifest, undoubted syphilis, find it positive in from 96 to 100 per cent. of the cases. There can be no doubt of its diagnostic value then in early as well as in later life.

But most of these observations have been made on cases of undoubted syphilis, cases in which the clinical signs left no doubt of the nature of the disease. Those making the observation have been engaged in "testing" the test, to see if it would "ring true"; to see if it would coincide with the clinical picture of well-known, easily recognized cases of the disease. They have proved beyond a doubt that the test does "ring true," that it does react positively in practically all cases with manifest signs of early congenital syphilis — "snuffles," skin lesions, mucous membrane lesions, etc. Indeed, in the very early cases, the reaction is apt to run closely hand-in-hand with the clinical signs; thus Mulzer and Michaelis report cases with suspicious family records, but themselves without physical signs, who gave soon after birth a negative serum reaction, and later, just before, or coincidentally with, the breaking out of characteristic signs, a positive reaction.

The use of the test, however, in other groups of cases, those of the obscure or latent type, as a valuable aid in determining the presence or absence of a syphilitic taint, has been little practiced. Comparatively few applications of the test have been made to cases which might be syphilis, yet are without sufficiently well-defined physical signs to warrant a positive diagnosis. One finds but few large series of these indefinite cases. Isolated examples of this or that condition are reported with either a positive or negative reaction, but not in sufficient number in a particular condition, e. g., arthritis, to justify conclusions as to the frequency of syphilis as a foundation cause of that condition.

Certain affections of the nervous system, however, have been studied with the test. Thus Knopfmacher and Schwalbe, studying the Wassermann reaction in hydrocephalus, collected twenty-nine cases, eight of which were positive (27 per cent.). They also quote some Danish workers who, among 2,000 cases of mental deficiency, practically all adults, found thirty-one giving a positive reaction. This series included 259 epileptics, only one of whom was positive.

Dean tested 330 cases, children or young adults, in a Potsdam asylum, and found positive results in fifty-one (15 per cent.). The most of these were idiots; they formed the bulk of the positive cases, forty-four of the fifty-one being in this class of patients. He also brings out the significant facts that of the fifty-one positive cases, only nine were clinically syphilis, four were suspected cases, and thirty-seven were entirely without signs of

the taint. Furthermore, he found that the proportion of positive cases diminished rapidly after 16 years of age, and suggests that a large percentage of positive results might be obtained in younger children. Dean quotes various authors, Ravait, Breton, Petit and Gayetoe, who have studied similar cases and have found from 9 to 30 per cent. giving a positive reaction.

Cases illustrating other conditions have been tested in but small numbers. They serve only to emphasize the fact that "symptomless" infants and children may give a positive reaction. Such are mostly very young infants, the offspring of parents known to be syphilitic; e. g., the cases already cited (Mulzer and Michaelis), also cases mentioned by Hochsinger: infants in whom the physician has reason to suspect a syphilitic inheritance and therefore has performed the serum test.

#### FIELD OF APPLICATION

There is a wide field for the use of the Wassermann serum test, as yet but little explored, in that class of patients frequenting our dispensaries and hospital wards. No extensive investigations of the serum test on a broad and comprehensive scale have yet been carried on among these patients. We are all familiar with the type: anemic, undersized, with lymph-nodes generally enlarged, often with a high lymphocyte count, they are generally below par, perhaps degenerate, and present a condition due to a great variety of causes, one of which *may* be syphilis. It is in this type of cases especially that the Wassermann test may be of great value, for its presence in such children is very strong evidence pointing toward a syphilitic foundation for their deteriorated, degenerate condition; its absence almost certain proof that syphilis does not exist.

#### OBJECTS OF THE PRESENT STUDY

It is with this class of children that this paper deals. The present study has been undertaken to determine, as far as possible, the following points:

1. What proportion of our hospital children will show a positive serum reaction?
2. What proportion of the positive cases present signs suggestive of syphilis?
3. Does a positive serum reaction in a child without characteristic physical signs mean syphilis?

The tests in the present series were made by Drs. W. E. Post, J. F. Waugh and H. K. Nicoll, and I wish to express my deep appreciation for the courtesy and skill of these gentlemen in thus making the work possible. Though not connected with the Hospital, they have given freely of their time and thought purely from "love of the cause" and interest



in an investigation which they as well as myself believe to be worth while, indeed even necessary. The work would have been impossible without their generous cooperation.

Tests were made on 102 infants and children, on six mothers and two fathers. On the children, 111 tests in all were made, twenty-eight Wassermann, eighty-three Noguchi. The blood was used in ninety cases, the spinal fluid in twelve cases. The children ranged in age from 3 days to 12 years; all, with but two exceptions, were patients at the Children's Memorial Hospital. There were thirty-nine positive reactions, sixty-two negative, and one case with a positive Noguchi but negative Wassermann. Thus 38 per cent. of the cases gave a positive reaction.

The mothers of the children in four positive cases were tested and gave one negative and three positive reactions; the one with the negative reaction had had the last one of three miscarriages two years before the test was made; she had had no specific treatment. The mothers of two negative-reacting children both gave negative results. Of the two fathers, one, with a positive-reacting child, himself gave a positive result. The second father was the parent of the 18-months-old infant with a positive Noguchi and negative Wassermann reaction and gave two negative Wassermanns, done by two different serologists a few days after the child was tested. No Noguchi was done on the father.

None of the 100 children entered the hospital as a case of syphilis. The admissions diagnoses are given in Table 1.

We note the great variety of diseases represented, involving practically all of the different systems of the body: nervous, circulatory, bony, respiratory, etc. But the affections which most attract attention by their positive results are those involving the nervous and circulatory systems, and the tuberculous infections. There are seventeen cases presenting diseases of the nervous system, with nine positive and eight negative reactions; sixteen cases of heart trouble, with seven positive and nine negative, and twenty-six tuberculous cases, with eight positive and eighteen negative reactions. There are fifteen cases affecting the respiratory system, five positive and ten negative. The remainder are scattered among the various conditions represented in Table 1. This table shows the varied character of the cases tested and also the proportion of positive cases. The number of cases, however, in a given condition is so small that the percentage of positive cases in such given condition cannot be considered as by any means an average percentage; this can be determined only by future investigations when large numbers of cases have been tested and analyzed.

Our chief interest of course is in the positive cases. These will now be considered in groups by themselves.

TABLE 1.—GIVING A SYNOPSIS OF ADMISSION DIAGNOSIS AND REACTIONS IN ALL CASES

Admission Diagnosis	Totals	Positive	Negative	Per cent. Positive
<b>Tuberculosis—</b>				
General .....	3	2	1	..
Meningeal .....	4	1	3	..
Pulmonary .....	2	1	1	..
Joints .....	17	4	13	31
	26	8	18	
<b>Nervous System—</b>				
Brain tumor .....	1	1	0	..
Little's disease .....	3	1	2	..
Encephalocele .....	1	0	1	..
Meningitis (meningococcus) ..	1	0	1	..
Meningitis, chronic .....	1	0	1	..
Microcephalus .....	1	1	0	..
Amaurotic family idiocy ...	1	1	0	..
Epilepsy .....	4	2	2	..
Spinal cord lesion .....	1	1	0	..
Poliomyeloencephalitis ....	2	1	1	..
Miscellaneous .....	1	1	0	..
	17	9	8	
<b>Circulatory System—</b>				
Congenital heart .....	5	2	3	40
Chronic endocarditis .....	11	5	6	45
	16	7	9	
<b>Respiratory System—</b>				
Rhinitis .....	1	1	0	..
Tonsils and adenoids .....	8	3	5	37
Bronchitis .....	1	0	1	..
Pneumonia .....	4	1	3	..
Asthma .....	1	0	1	..
	15	5	10	
<b>Digestive System—</b>				
Hare-lip .....	5	1	4	20
Enteritis .....	5	1	4	20
	10	2	8	
<b>Osseous System—</b>				
Arthritis periostitis .....	1	1	0	..
Osteomyelitis .....	1	1	0	..
Club-foot .....	2	0	2	..
Fractured toe .....	1	0	1	..
	5	2	3	
<b>Miscellaneous—</b>				
Anemia .....	2	1	1	..
Keratitis .....	3	2	1	..
Phimosis .....	1	1	0	..
Rachitis .....	5	1	4	20
Still's Disease .....	1	1	0	..
Typhoid fever .....	1	0	1	..
	13	6	7	
<b>Totals .....</b>	<b>102</b>	<b>39</b>	<b>63</b>	<b>38</b>

## POSITIVE CASES

The total number of cases giving a positive reaction is thirty-nine, ranging in age from 1 week to 12 years, distributed as follows:

Age, Years	No. of Cases	Age, Years	No. of Cases
Under 1 .....	5	7 .....	4
Between 1 and 2 .....	4	8 .....	3
2 .....	1	9 .....	4
3 .....	4	10 .....	2
4 .....	4	11 .....	3
5 .....	2	12 .....	2
6 .....	1		

There were twenty-five boys and fourteen girls.

## METHOD OF STUDY

The cases have been studied from the following points of view: the admission diagnosis, the family history, the patient's own previous record of development and general health, the physical condition at the time of making the test, and, in the fatal cases, the results of autopsy. Information along these lines seemed necessary in order to "check up" the test and to answer the second and third questions. Details of the cases are given in Table 3.

The admission diagnoses are given in Table 2. Study of this table shows that of the thirty-nine positive reactions, 8 were obtained in tuberculous trouble, 9 in affections of the nervous system, 5 respiratory, 7 circulatory, 2 osseous, 2 digestive, and 6 were in miscellaneous conditions.

The family history was investigated with special reference to syphilis. It shows a positive record of this disease in four cases, a suggestive record in sixteen cases, a negative one in eighteen cases, no history obtainable in two cases. By a "positive" record is meant a definite history of clinical syphilis in another member of the family or a positive Wassermann reaction in either parent; by a "suggestive" record is meant a history of miscarriage in the mother, of serious mental or nervous trouble in another member of the family, or the occurrence of a positive reaction in a brother or sister not of adult age. Thus, of the thirty-nine cases twenty-one (56 per cent.) show a family history conclusive or suggestive, of a syphilitic taint. Only 20 per cent. of the negative cases show such family history.

The family history is often such an important factor in arriving at a diagnosis of congenital syphilis, that it has seemed worth while thus to consider it by itself with reference to the serum reaction in the positive cases. But the personal record and the physical condition of the child himself must, after all, finally determine the question. The cases, therefore, have been studied with reference to the combination of all three of

TABLE 2.—ADMISSION DIAGNOSES IN THE POSITIVE CASES

Tuberculosis—		No. of Cases
General .....		2
Joints .....		4
Meningeal .....		1
Pulmonary .....		1
Total .....		8
Nervous System—		
Brain tumor .....		1
Little's disease .....		1
Microcephalus .....		1
Amaurotic family idiocy .....		1
Epilepsy .....		2
Spinal cord, lesion of? .....		1
Poliomyeloencephalitis .....		1
Miscellaneous nervous .....		1
Total .....		9
Respiratory System—		
Rhinitis .....		1
Tonsils and adenoids .....		3
Pneumonia .....		1
Total .....		5
Circulatory System—		
Congenital heart .....		2
Chronic endocarditis .....		5
Total .....		7
Osseous System—		
Periostitis .....		1
Osteomyelitis .....		1
Total .....		2
Digestive System—		
Hare-lip, etc. ....		1
Enteritis .....		1
Total .....		2
Miscellaneous—		
Anemia .....		1
Keratitis .....		2
Phimosis .....		1
Rachitis .....		1
Still's disease .....		1
Total .....		6
Grand Total .....		39

these factors, i. e., family history, personal record and physical examination, in order to see to what extent these factors and the serum reaction coincide. For this purpose they will now be rearranged in five separate groups.

Group I.—Cases with family history, personal record and physical signs, all suggestive, or even diagnostic, of syphilis. There are nine of these cases.

Group II.—Cases with either family or personal history, plus physical signs, suggestive of syphilis. There are nine of these cases.

Group III.—Cases with only physical signs suggestive of syphilis. There are six of these cases.

Group IV.—Cases with either a suggestive family history alone, or a suggestive personal record alone. There are five of these cases.

Group V.—Cases without either family history, personal record or physical signs suggestive of syphilis. There are ten of these cases.

The cases of Groups I, II and III may all be regarded as clinically syphilis. All of these, twenty-four in number, or 63 per cent. of the positive cases, give suggestive physical signs. Among the negative cases only 5 per cent. give such suggestive signs. Cases of Group IV, in view of either a positive family history or positive personal record plus a positive serum reaction, are probably syphilitic, making in all, twenty-nine cases, or 28 per cent. of the whole series, which are probably syphilis.

Group V is an important group and requires special discussion, but before proceeding with that discussion, certain cases in the other groups are of interest.

GROUP I.—Cases 26 and 27 were twin brothers who entered the Hospital for the removal of tonsils and adenoids. Both were undersized though of different weights; each had a goiter. The mother had had three miscarriages since the birth of the twins but gave, at this time, a negative Noguchi reaction. The twins were put on mercurial treatment, Nov. 11, 1911, and began to improve immediately, the more vigorous one faster than his brother; the former went from 52½ pounds, Feb. 16, 1912, up to 54½ pounds, March 23, 1912, and on the latter date had a negative reaction; his brother, between the same dates, went from 50 pounds to 51½ pounds and still gave a positive reaction. The more vigorous one of these twins thus gave evidence of greater resistance to his hereditary taint, not only by the improvement in his general physical condition, but by the change of his positive reaction into a negative one.

Cases 35 and 36 were also brothers, instances, again, of "familial" syphilis, each showing a keratitis, one also an arthritis and one also deafness. Both left the hospital unimproved after three weeks' treatment with mercurials; five months later the arthritis one returned with his keratitis much worse and his serum reaction still positive. He is now under observation, improving under vigorous mercurial treatment.

GROUP III.—Case 34 was an anemic, 18-months-old infant in private practice; she was backward about her teeth, was fat and "flabby," had a lymphocytosis and a dactylitis. Her blood gave a markedly positive Noguchi reaction. One of the leading syphilographers of Chicago saw her with me in consultation, could not accept the specificity of the Noguchi reaction, doubted the diagnosis of syphilis, and suggested a

straight Wassermann test. This was done and was reported negative. Calomel, one-tenth gr. t. i. d. for four days had been given after the Noguchi and before the Wassermann test, but it is improbable that this small amount of mercury converted a positive into a negative reaction. The tests were done by different serologists, both skilful and expert workers. The father was an educated man, appreciated the importance of the truth, denied syphilis, and his blood gave a negative Wassermann reaction, the test being made by the man who found the negative reaction in the child. No Noguchi was done on the father.

GROUP IV.—Case 3, a 3-year-old child, entered the Hospital as a case of tuberculous meningitis. The father gave a history of "soft" chancre seven years before (i. e., four years before the birth of the patient), the mother a history of one miscarriage (date ?); and of a baby younger than the patient who had always been "delicate with heart trouble" and who died at 1 year. The patient's spinal fluid gave a strong Noguchi reaction. The autopsy showed a marked tuberculous meningitis, with tubercle bacilli present in great numbers in the exudate at the base of the brain. There were no lesions of syphilis, either gross or microscopic; no spirochetes in the meningeal exudate examined by the Levaditi method. The head only was examined.

GROUP V.—The cases of this group cannot be regarded as clinically syphilis in the ordinary sense of the term, and such a diagnosis would rest largely on the results of the serum test; in these cases the test was positive. Are we, then, to accept such a result as evidence of the presence of syphilis? Are we to regard as cases of syphilis, patients who, without suspicious family history, without suggestive personal record or physical signs, yet nevertheless give a positive serum reaction? How are we to explain the positive reaction in such patients?

There are three possible explanations:

1. The reaction is correct and is due to some condition other than syphilis.
2. The reaction is correct and is due to syphilis, which may be the real underlying cause of the condition named, or may be a factor predisposing toward some other infection, e. g., tuberculosis.
3. The reaction is incorrect, due to some error of technic.

The first supposition, that the reaction is due to some condition other than syphilis, is untenable. Aside from syphilis, the only conditions in which a positive Wassermann reaction has been found are scarlet fever, jaundice, leprosy, carcinoma, diabetes mellitus and possibly malaria. None of these conditions existed in any of the cases in Group V; furthermore, there is no ground for believing that any of the conditions named in this group would cause a reaction of such specificity as is the Wassermann reaction.

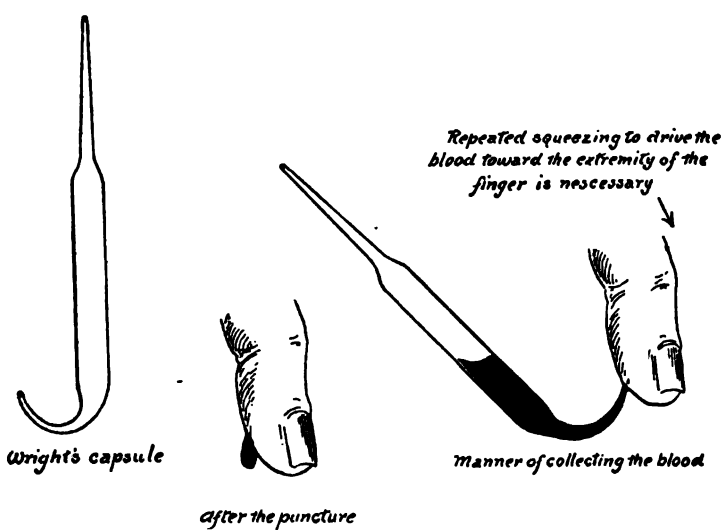


Fig. 1.—Method of collecting blood from the finger-tip by means of a Wright capsule. (From Noguchi: The Serum Diagnosis of Syphilis, 1912.)

ILLUSTRATING ARTICLE BY  
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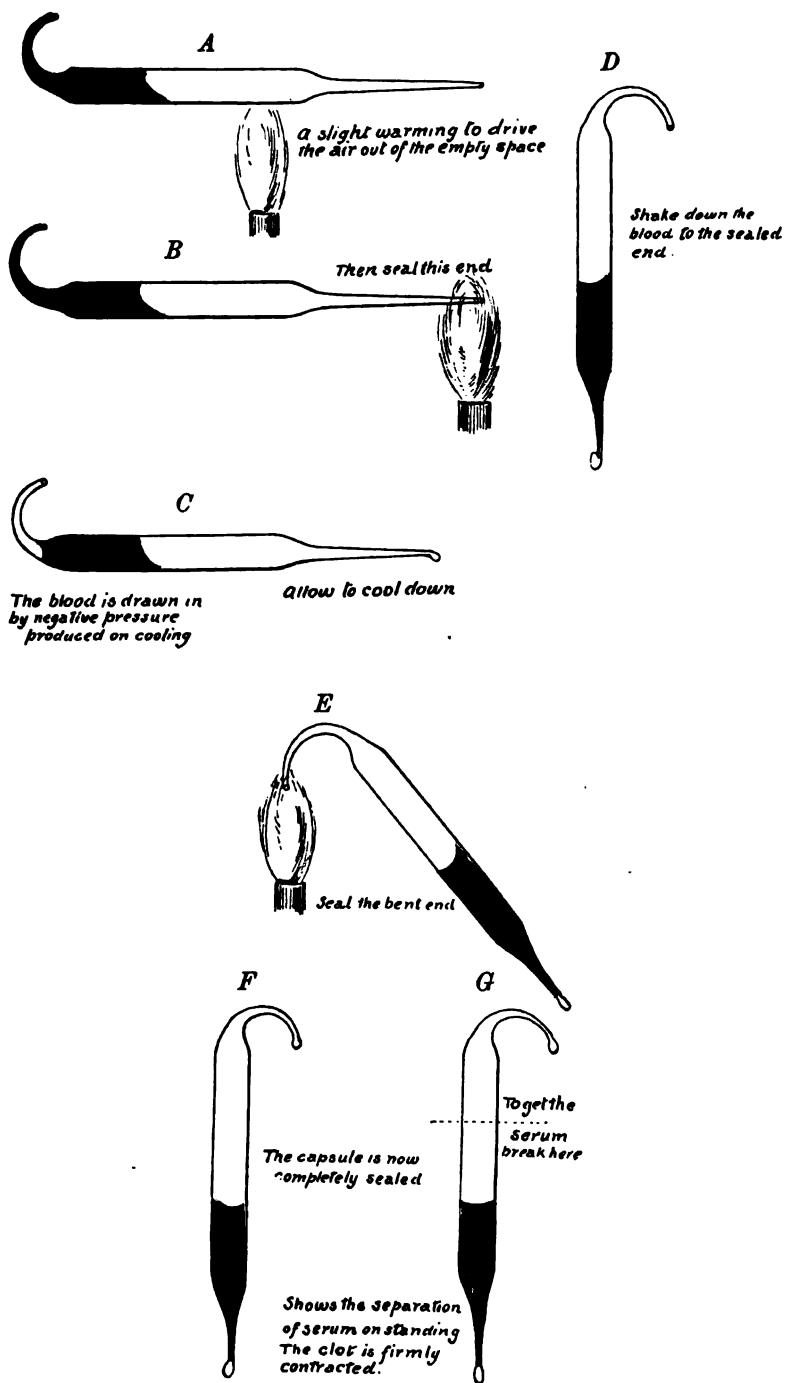


Fig. 2.—Showing the further steps in the technic of collecting the blood and obtaining the serum in the serum test for syphilis. (From Noguchi: The Serum Diagnosis of Syphilis, 1912.)



The second supposition, that the reaction is correct and is due to syphilis, the physical conditions found being either unusual manifestations of syphilis or coexisting as separate entities, e. g., tuberculosis, is debatable.

Syphilis is of course a most protean disease. Not a single tissue of the body is there that may not be attacked by the virus, once the latter has gained access to the body. Its obscurity and latency at times are well known. Especially in congenital syphilis may its manifestations be most varied. They may furthermore be latent for a period, giving rise to no symptoms or signs, yet later showing characteristic stigmata of the disease, the so-called *syphilis hereditaria tarda*. It is conceivable that the cases in Group V may belong to this class; that they are cases of latent, late syphilis and that they may show active signs of the disease later on in life, perhaps at puberty. Before the advent of the serum test it would not have occurred to any clinician examining these patients to regard them as syphilitic. He would have classified them as above, and their anemia, lymphocytosis, adenitis and general deterioration he would have attributed to general causes—bad hygiene, bad food, lack of care, etc. But among the causes to which these conditions *may* be due is the specific cause syphilis; hence, finding these conditions present, finding also present a test so strongly diagnostic of syphilis as is the serum test, it is entirely possible that these cases in Group V may be syphilitic, that they are in reality cases of hereditary syphilis, in a latent stage; cases in which the disease process is so sluggish that it has as yet given rise to no gross, evident sign characteristic of the taint, yet active enough to produce a more or less deteriorated condition and a positive result when tested by the delicate serum reaction.

This reasoning, however, cannot, I believe, apply to the three fatal cases in the group, Cases 12, 31 and 38. Cases 31 and 38 came to autopsy and showed no signs gross or microscopic of syphilis. No spirochetes were detected in the liver in either case. The heart muscle was not examined for the spirochetes, and it is possible, in view of recent investigations, notably by Warthin, that they might have been found in the tissues of that organ. The third fatal case, Case 12, was one of amaurotic family idiocy; it gave a negative reaction, June 26, 1910, a positive one six months later, Jan. 22, 1911, both tests being made by the same serologist. No autopsy was obtained, but the autopsies which have been made on cases of this disease do not mention syphilitic changes in the tissues. Syphilis seems improbable in our case. Noguchi,<sup>1</sup> page 134, alludes to one case of amaurotic family idiocy with a negative reaction.

Case 1 must also be questioned. No definite diagnosis was made. The patient was a 3-year-old child who came in after a three weeks' illness with typhoidal symptoms; Widal reaction, blood culture and Pirquet test were all negative. It was probably a case of miliary tuberculosis.

TABLE 3.—CASES SHOWING POSITIVE SERUM REACTION

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
1	3	M	Miliary Tuberculosis?	Uncle died of phthisis	Always delicate; typhoid symptoms 3 weeks.	Emaciation; glands +; spleen +; T. 98-104 F.; blood culture neg. Widal negative.	Noguchi +	Pirquet negative left in 1 wk; unimproved.
2	12	M	General debility Tb. ? 11/14/10	Mother had 3 or 4 miscarriages; 7 other children well.	Developm't backward; dull mentally; pneumonia 4 years ago; scarlet fever 2 years ago; measles 2 years ago.	Poor development; glands +.	Noguchi + 11/28/10	Pirquet + 11/28/10
3	3	M	Tb. Meningitis 4/4/12	Father had "soft chancre" 7 years before; mother had one miscar.; younger brother died one year ago of "heart trouble"; all ways delicate.	Gen. development normal; present illness began 7 weeks ago.	Typical meningeal signs; Sp. Fl. clear; lymphocytes; Tb. bacilli? Pirquet negat. Double otitis media.	Sp. Fl. + Noguchi +++	Died 4/8/12. Autopsy (on head only) showed tb. meningitis, bacilli in exudate at base of brain; no syphilitic changes.
4	1½	F	Broncho-Pneumonia Tb. ?	Mother had one miscarriage before birth of patient.	Developm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands +; bronchitis; consolidation ? tonsils +; spleen +.	+	Pirquet ++

5	7	M	Tb. Hip	Negative	Measles 1 yr. ago; pertussis; date ? Fall 3 wks. ago; R. hip tender since; lame.	Nutrition good; glands +; teeth irreg. and notched; R. hip tender.	Noguchi +	Pirquet negative
6	4	F	Tb. Knee	Negative	Development normal; knee symptoms 3 mos.	Pale, nutrition fair; tonsils +.	Wassermann +	Pirquet ++
7	5	F	Tb. Spine 7/15/10	Negative	Pertussis at 1 year; present trouble began 1½ years ago.	Spinal deformity; glds. +; consolidation R. lung, post. on 1/6/11.	Noguchi + 2/1/11	
8	4	M	Tb. Spine 5/5/11	?	Measles 1 yr. ago and since, pain in back and can not walk.	Pale, nutrition poor. Chest: enlarged bronchial glands ? Abdomen: Tb. ? nodules; spleen +; liver +; choked disks (1/20/12, 2/21/12); T. 97-102 F.	Wassermann + 2/24/12	Has had tuberculosis regularly since admission to date
9	11	M	Papillitis 1/17/11 Intracranial tumor	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoordination; ataxic gait; paralysis of L. abductens; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
10	3	M	Little's disease	?	Always delicate, measles, date ? meningial symptoms for 2 wks.	Nutrition poor; rigidities; glands +; rickets signs.	Noguchi — 9/5/10 Noguchi + 1/19/11	Pneumonia 1/13/11 Antitoxin.
11	7	F	Microcephalus 1/9/11	Mother had one still-born, one abortion, then the patient and since two still-born.	Backward. Pneumonia at 2 years.	Nutrition poor; physical and mental development backward; tonsils+; head small.	Noguchi + 1/11/11	

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Diagnosis Admission	Family History	Previous History	Examination	Reaction	Remarks
12	4	M	Amaurotic family idiocy 6/24/10	Negative	Always delicate; at 1 week vomiting and convulsions.	Emaciation; eyes show characteristic changes; glands +.	Noguchi — 6/26/10 Noguchi + 1/22/11	Death 9/8/11
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, migraine and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Measles and pertussis in infancy; diphtheria 2 years ago; characteristic seizures since 7-8 mos. old.	Parietal bosses ++; nose flattened; tonsils +; glands +.	Noguchi ++ 2/27/11	
14	8	M	Epilepsy 3/18/11	Epilepsy in maternal G. M. Mother had petit mal? 3 other children well.	Labor instrumental; mentally slow; measles and scarlet fever 4 yrs. ago; varicella 2 mos. ago; pneumonia 3 mos. ago; "spells" for 2 years.	Head asymmetrical; otitis; pigeon-breast.	Noguchi + 3/9/11	
15	10	F	Lesion of spinal cord 9/30/10	Negative	Weak at birth; measles at 7 years; varicella at 9 years; fall 1 yr. ago; since spinal symptoms.	Nutrition poor; paresis R. limbs; teeth notched; glands ++; patellar ++; tonsils and adenoids removed; no spirochetes found.	Noguchi + 10/6/10	

16	11	F	Poliomyelencephalitis	Negative	Pneumonia; date ? Typhoid date ? Unable to walk for 2 yrs.	Teeth notched and decayed; tonsils +; spastic lower limbs.	Noguchi + 2/9/11	
17	3	M	Backward speech 12/17/10	Father had chancre; autopsy showed syphilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; younger brother has neg. Noguchi. Paternal g. f. had syphilis?	Developm't slow; bronchopneumonia at 2½ years.	Nervous, pale; development poor; can't talk; liver +.	Noguchi + 12/19/10	Pirquet ++
18	½	M	Congenital heart disease 1/4/11	Mother had miscarriage 5 years ago; 3 other child'n healthy; mother died 1 week ago of pneumonia and endocarditis.	Full term, instruments, condition good. Pertussis 3 mos. ago followed by pneumonia. Double otitis, 1 mo.	Nutrition poor; organic heart-signs; ears discharging; weight 10 lbs., 2 oz.	Noguchi + 2/9/11	Left 7/3/11 Mercury from 2/28/11 to 4/6/11
	1¼		10/27/11			Reentered in collapse		Blood and Sp. Fl. from autopsy negative, by both Wassermann and Noguchi. No syphilitic changes in tissues
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Developm't and nutrition poor; bronchopneumonia; organic heart murmur; spleen +; liver ++.	Noguchi + 12/1/10	Recovery from pneumonia. Died July, 1911, at home.

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Reaction
20	8	M	Endo-pericarditis 3/15/11	Father died phthisis, 2 years ago.	Weak since 5 yrs. old; measles and diphtheria; rheumatism 1 yr. ago; for 1 mo. cough, pain in chest, weakness, dyspnea.	Pale, nutrition fair; tonsils +, glands +. Endopericarditis.	Noguchi Doubtful—3/29/11 Weakly + 4/6/11 Positive 5/11/11	
21	6	F	Endocarditis, mitral aortic? 9/10/11	Father has Noguchi +++ on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs. ?	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyart. rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11
23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands +; liver +; no spleen.	Noguchi + (weak)	



24	7	F	Endopercarditis 7/21/11	Mother had 2 miscarriages; poor health since last baby, five years ago.	Measles at 11 mos.; scarlet fever at 4 yrs. Sore throat frequently; for 3 weeks abdominal pain.	Nutrition poor; pale; tonsils +; pericarditis; mitral murmur.	Noguchi + 8/6/11	Left improved 7/17/10
25	1/4	F	Rhinitis — "snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands +; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	
26	9	M	Tonsils and adenoids	Mother had miscarriages 1 1/2 yr., 4 yrs. and 7 yrs. after birth of twin patients.	Developm't backward; pertussis and mumps at 18 mos.; measles at 6 yrs.; recurrent tonsillitis.	Developm't and nutrition poor; pale; tonsils +; thyroid +; glands +.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi + 3/23/12	
27	9	M	Tonsils and adenoids	Mother: Noguchi negative. Twin brother of Case 26.	As in brother.	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi — 3/23/12	
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Vari- cella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils +; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	
29	2	M	Lobar pneumonia	Negative.	Pneumonia at 1 year.	Nutrition poor; pale; nose flat; vacant stare and "grin"; tonsils +.	Wassermann + 2/19/12	Pirquet negative 2/19/12

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguchi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
31	1/6	M	Enterocolitis, Convulsions	Negative.	Well at birth; "cold" for 10 days; convulsions for 24 hours.	Emaciation, pallor; moribund. Sp. Fl. neg. for bacteria; Sp. Fl. pos. for Noguchi.	Blood post-mortem gave positive Noguchi	Autopsy 10 hrs. after death; no signs of syphilis.
32	11	F	Fracture of ulna 10/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands +; old scars on both shins. Fracture of L. ulna; x-ray shows multiple periostitis in both upper limbs.	Noguchi + 12/6/10	Discharged 1/27/11 Improved on Hg.
33	7	M	Osteomyelitis 3/27/10 Readmitted 12/7/10	Negative	Measles at 1½ years; scarlet fever at 3½ years; for 7 mos. pain in legs, fever, sweating.	Nutrition fair; both tibiae have discharging sinuses. As above.	Noguchi + 12/20/10	Disch'd 9/10/10 Improved Given Hg and KI Improved.
34	1½	F	Anemia	Negative. Father had 2 negative Wassermans.	Normal development. For 3 weeks daily rise of temperature; cause?	Pale; nose flat; tonsils +; dactylitis.	Noguchi + 1/7/11 Wassermann — 1/17/11	Calomel. Tests by different men.

\*17 days.

35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguchi + 9/22/10	Discharged 10/8/10 No treatment since discharge.
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguchi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguchi + 3/15/12	
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguchi + 12/18/11	
38	1½	M	Rachitis gastroenteritis 6/29/10	Negative.	Negative	Developm't and nutrition poor; rachitic signs; spleen +.	Noguchi ++ 11/28/10	Pirquet negative. Died 2/11/11. Autopsy showed no gross nor microscopic signs of syphilis.
39	5	F	Still's disease	Negative.	Measles 3 years ago; pertussis 2 years ago; for 1 year pain in limbs and joints; unable to walk.	Nutrition poor; rachitic changes; swelling and stiffness of joints.	Noguchi + 10/24/10 1/9/11 Noguchi — 1/19/11	Hg and KI from Oct. to March, 1911.

TABLE 4. CASES IN TABLE 2 GROUPED WITH REFERENCE TO THE RELATION OF FAMILY HISTORY, PERSONAL RECORD AND PHYSICAL EXAMINATION TO THE SERUM TEST, POSITIVE CASES

GROUP 1

No. of Cases	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, syphilis and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Meningitis and petechiae in infancy; diphtheria 2 years ago; chronic focal seizure since 7 1/2 mos. old.	Partial brownness of nose flattened; tonsils ++ glands ++.	Negative 2/27/11	
11	7	F	Microcephalus 1/9/11	Mother had one still born, one abortion, then the patient and since two still born.	Backward. Pneumonia at 2 years.	Nutrition poor; physical and mental development backward; tonsils ++ head small.	Negative 1/11/11	
17	8	M	Backward speech 12/17/10	Father had characteristic autopsy showed syphilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; young brother has neg. Noguchi. Paternal gr. had syphilis?	Development slow; bronchopneumonia at 2 1/2 years.	Neurotic, pale; development poor; can't talk; liver ++.	Negative 12/19/10	Pharynx ++
20	9	M	Tonsils and adenoids	Mother had miscarriages 1 1/2 yrs., 4 yrs., and 7 yrs. after birth of twin patients.	Development backward; petechiae and nodule at 18 mos.; nodule at 6 yrs.; recurrent tonsillitis.	Development and nutrition poor; pale; tonsils ++ thyroid ++ glands ++.	Negative 11/9/11 Negative 12/20/11 Negative 1/26/12 Negative 8/23/12	

27	9	M	Tonsils and adenoids	Mother: Noguechi negative. Twin brother of Case 26.	As in brother.	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguechi + 11/9/11 Noguechi + 12/20/11 Noguechi + 2/26/12 Noguechi — 3/23/12	
35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguechi + 9/22/10	
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguechi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguechi + 3/15/12	Discharged 10/8/10 No treatment since discharge.
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguechi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguechi + 12/18/11	

\*17 days.

TABLE 4.—CONTINUED  
GROUP II

Case No.	Age Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
4	1½	F	Broncho-Pneumonia Tb.?	Mother had one miscarriage before birth of patient.	Devel'pm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands +; bronchitis; consolidation; tonsils +; spleen +.	+	Pirquet ++
9	11	M	Papillitis 1/17/11 Intracranial tumor	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoordination; ataxic gait; paralysis of L. abducens; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
21	6	F	Endocarditis, mitral, aortic? 9/10/11	Father has Noguchi +++ on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs. ?	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral, aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 6 mos. ago, followed by polyarticular rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/16/10	Died 4/9/11

23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands ++; liver ++; no spleen.	Noguchi + (weak)	Recovery from pneumonia. Died July, 1911, at home.
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Developm't and nutrition poor; bronchopneumonia; organic heart murmur; spleen ++; liver ++.	Noguchi + 12/1/10	
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Vari- cella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils ++; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	
25	¾	F	Rhinitis — "snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands ++; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	Left improved 7/17/10
32	11	F	Fracture of ulna 11/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands ++; old scars on both shins. Fracture of L. ulna; x-ray shows multiple periostitis in both upper limbs.	Noguchi + 11/30/10	Discharged 1/27/11 Improved on Hg.

TABLE 4.—CONTINUED  
GROUP II

Case No.	Age Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
4	1½	F	Broncho-Pneumonia Tb.?	Mother had one miscarriage before birth of patient.	Devel'pm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands +; bronchitis; consolidation; tonsils +; spleen +.	+	Pirquet ++
9	11	M	Papillitis 1/17/11 Intracranial tumor	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoordination; ataxic gait; paralysis of L. abductens; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
21	6	F	Endocarditis, mitral, aortic? 9/10/11	Father has Noguchi +++ on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs.?	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral, aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyartic. rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11



23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands ++; liver ++; no spleen.	Noguchi + (weak)	Recovery from pneumonia. Died July, 1911, at home.
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Developm't and nutrition poor; bronchopneumonia; organic heart murmur; spleen ++; liver ++.	Noguchi + 12/1/10	
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Vari- cella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils ++; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	
25	¼	F	Rhinitis — "snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands ++; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	Left improved 7/17/10
32	11	F	Fracture of ulna 11/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands ++; old scars on both shins. Fracture of L. ulna; x-ray shows multiple periostitis in both upper limbs.	Noguchi + 11/30/10	Discharged 1/27/11 Improved on Hg.

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Diagnosis Admission	Family History	Previous History	Examination	Reaction	Remarks
12	4	M	Anaurotic family idiocy 6/24/10	Negative	Always delicate; at 1 week vomiting and convulsions.	Emaciation; eyes show characteristic changes; glands +.	Noguchi — 6/26/10 Noguchi + 1/22/11	Death 9/8/11
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, migraine and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Measles and pertussis in infancy; diphtheria 2 years ago; characteristic seizures since 7-8 mos. old.	Parietal bosses +; nose flattened; tonsils +; glands +.	Noguchi ++ 2/27/11	
14	8	M	Epilepsy 3/18/11	Epilepsy in maternal G. M. Mother had petit mal? 3 other children well.	Labor instrumental; mentally slow; measles and scarlet fever 4 yrs. ago; varicella 2 mos. ago; pneumonia 3 mos. ago; "spells" for 2 years.	Head asymmetrical; otitis; pigeon-breast.	Noguchi + 3/9/11	
15	10	F	Lesion of spinal cord 9/30/10	Negative	Weak at birth; measles at 7 years; varicella at 9 years; fall 1 yr. ago; since spinal symptoms.	Nutrition poor; paresis R. limbs; teeth notched; glands ++; patellar ++; tonsils and adenoids removed; no spirochetes found.	Noguchi + 10/5/10	

16	11	F	Poliomyelencephalitis	Negative	Pneumonia; date ? Typhoid date ? Un- able to walk for 2 yrs.	Teeth notched and de- cayed; tonsils ++; spastic lower limbs.	Noguchi + 2/9/11	
17	3	M	Backward speech 12/17/10	Father had chancre; autopsy showed syph- ilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; young- er brother has neg. Noguchi. Paternal g. f. had syphilis?	Developm't slow; bron- chopneumonia at 2½ years.	Nervous, pale; devel- opment poor; can't talk; liver +.	Noguchi + 12/19/10	Pirquet ++
18	½	M	Congenital heart disease 1/4/11	Mother had miscar- riage 5 years ago; 3 other child'n healthy; mother died 1 week ago of pneumonia and endocarditis.	Full term, instruments, condition good. Per- tussis 3 mos. ago fol- lowed by pneumonia. Double otitis, 1 mo.	Nutrition poor; or- ganic heart-signs; ears discharging; weight 10 lbs., 2 oz.	Noguchi + 2/9/11	Left 7/3/11 Mercury from 2/28/11 to 4/8/11
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/ 28/10.	Always delicate.	Reentered in collapse	Noguchi + 12/1/10	Blood and Sp. Fl. from autopsy negative, by both Wassermann and Noguchi. No syphilitic changes in tissues  Recovery from pneumonia. Died July, 1911, at home.

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Reaction
20	8	M	Endo-pericarditis 3/15/11	Father died phthisis, 2 years ago.	Weak since 5 yrs. old; measles and diphtheria; rheumatism 1 yr. ago; for 1 mo. cough, pain in chest, weakness, dyspnea.	Pale, nutrition fair; tonsils +, glands +. Endopericarditis.	Noguchi Doubtful—3/29/11 Weakly + 4/6/11 Positive 5/11/11	
21	6	F	Endocarditis, mitral aortic? 9/10/11	Father has Noguchi + + + on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs. ?	Wassermann + 2/13/12	Pirquet + + +
22	10	F	Endocarditis, mitral aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi + +.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyart. rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11
23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils + +; teeth irregular, notched; mitral murmur; glands +; liver +; no spleen.	Noguchi + (weak)	

24	7	F	Endopericarditis 7/21/11	Mother had 2 miscarriages; poor health since last baby, five years ago.	Measles at 11 mos.; scarlet fever at 4 yrs. Sore throat frequently; for 3 weeks abdominal pain.	Nutrition poor; pale; tonsils +; pericarditis; mitral murmur.	Noguchi + 8/6/11	Left improved 7/17/10
25	1/4	F	Rhinitis — "snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands +; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	
26	9	M	Tonsils and adenoids	Mother had miscarriages 1 1/2 yr., 4 yrs. and 7 yrs. after birth of twin patients.	Developm't backward; pertussis and mumps at 18 mos.; measles at 5 yrs.; recurrent tonsillitis.	Developm't and nutrition poor; pale; tonsils +; thyroid +; glands +.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi + 3/23/12	
27	9	M	Tonsils and adenoids	Mother: Noguchi negative. Twin brother of Case 26.	As in brother.	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi — 3/23/12	
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 6 living children.	Measles, date ? Vari- cella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils +; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	
29	2	M	Lobar pneumonia	Negative.	Pneumonia at 1 year.	Nutrition poor; pale; nose flat; vacant stare and "grin"; tonsils +.	Wassermann + 2/19/12	Pirquet negative 2/19/12

TABLE 3.—CONTINUED

Case No	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguchi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
31	1/6	M	Enterocolitis, Convulsions	Negative.	Well at birth; "cold" for 10 days; convulsions for 24 hours.	Emaciation, pallor; moribund. Sp. Fl. neg. for bacteria; Sp. Fl. pos. for Noguchi.	Blood post-mortem gave positive Noguchi	Autopsy 10 hrs. after death; no signs of syphilia.
32	11	F	Fracture of ulna 10/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands +; old scars on both shins. Fracture of L. ulna; x-ray shows multiple periostitis in both upper limbs.	Noguchi + 12/8/10	Discharged 1/27/11 Improved on Hg.
33	7	M	Osteomyelitis 3/27/10 Readmitted 12/7/10	Negative	Measles at 1½ years; scarlet fever at 3½ years; for 7 mos. pain in legs, fever, sweating.	Nutrition fair; both tibiae have discharging sinuses. As above.	Noguchi + 12/20/10	Disch'd 9/10/10 Improved Given Hg and KI Improved.
34	1½	F	Anemia	Negative. Father had 2 negative Wassermanns.	Normal development. For 3 weeks daily rise of temperature; cause ?	Pale; nose flat; tonsils +; dactylitis.	Noguchi + 1/7/11 Wassermann — 1/17/11	Calomel. Tests by different men.

\*17 days.

35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguchi + 9/22/10	Discharged 10/8/10 No treatment since discharge.
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguchi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguchi + 3/15/12	
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguchi + 12/18/11	
38	1 1/2	M	Rachitis gastroenteritis 6/29/10	Negative.	Negative	Developm't and nutrition poor; rachitic signs; spleen +.	Noguchi ++ 11/28/10	Pirquet negative. Died 2/11/11. Autopsy showed no gross nor microscopic signs of syphilis.
39	5	F	Still's disease	Negative.	Measles 3 years ago; pertussis 2 years ago; for 1 year pain in limbs and joints; unable to walk.	Nutrition poor; rachitic changes; swelling and stiffness of joints.	Noguchi + 10/24/10 1/9/11 Noguchi — 1/19/11	Hg and KI from Oct. to March, 1911.

TABLE 4.—CASES IN TABLE 2 GROUPED WITH REFERENCE TO THE RELATION OF FAMILY HISTORY, PERSONAL RECORD AND PHYSICAL EXAMINATION TO THE SERUM TEST. POSITIVE CASES

GROUP I

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, migraine and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Measles and pertussis in infancy; diphtheria 2 years ago; characteristic seizures since 7-8 mos. old.	Parietal bosses +; nose flattened; tonsils +; glands +.	Noguchi ++ 2/27/11	
11	7	F	Microcephalus 1/9/11	Mother had one still-born, one abortion, then the patient and since two still-born.	Backward. Pneumonia at 2 years.	Nutrition poor; physical and mental development backward; tonsils +; head small.	Noguchi + 1/11/11	
17	3	M	Backward speech 12/17/10	Father had chancre; autopsy showed syphilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; younger brother has neg. Noguchi. Paternal g. f. had syphilis?	Developm't slow; bronchopneumonia at 2½ years.	Nervous, pale; development poor; can't talk; liver +.	Noguchi + 12/19/10	Pirquet ++
26	9	M	Tonsils and adenoids	Mother had miscarriages 1½ yr., 4 yrs. and 7 yrs. after birth of twin patients.	Developm't backward; pertussis and mumps at 18 mos.; measles at 5 yrs.; recurrent tonsillitis.	Developm't and nutrition poor; pale; tonsils +; thyroid +; glands +.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/20/12 Noguchi + 3/23/12	



27	9	M	Tonsils and adenoids	Mother: Noguchi negative. Twin brother of Case 26.	As in brother.	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi — 3/23/12	
35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguchi + 9/22/10	
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguchi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguchi + 3/15/12	Discharged 10/8/10 No treatment since discharge.
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguchi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguchi + 12/18/11	

\*17 days.

TABLE 4.—(CONTINUED)  
GROUP II

Case No.	Age Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
4	1½	F	Broncho-pneumonia Tb.?	Mother had one miscarriage before birth of patient.	Devel'm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands +; bronchitis; consolidation; tonsils +; spleen +.	+	Pirquet ++
9	11	M	Pyelitis 1/17/11 Intracranial tumor	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoordination; ataxic gait; paralysis of L. abdomen; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
21	6	F	Endocarditis, mitral, aortic? 9/10/11	Father has Noguchi +++ on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmur, aortic murmur.	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral, aortic? 11/22/10	Mother has gonorrhea; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyarthritis, rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmur; aortic murmur; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11

23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands ++; liver ++; no spleen.	Noguchi + (weak)	Recovery from pneumonia. Died July, 1911, at home.
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Development poor; bronchopneumonia; organic heart murmur; spleen ++; liver ++.	Noguchi + 12/1/10	
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Varicella, date ? Repeated sore throat; adenoid symptoms.	Development poor; pale; tonsils ++; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	
25	¼	F	Rhinitis — "snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands ++; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	Left improved 7/17/10
32	11	F	Fracture of ulna 11/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands ++; old scars on both shins. Fracture of L. ulna; x-ray shows multiple periostitis in both upper limbs.	Noguchi + 11/30/10	Discharged 1/27/11 Improved on Hg.

TABLE 4. CONTINUED  
GROUP III

No.	Age, years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
5	7	M	Tb. Hip	Negative	Mouse 1 yr. ago; per- tussis; date ? full 3 wks. ago; R. hip tender since; lame.	Nutrition good; glands +; teeth irreg. and notched; R. hip ten- der.	Noguchi +	Pirquet negative
6	4	M	Tb. Spine 5/5/11	?	Mouse 1 yr. ago and since, pain in back and can not walk.	Pale, nutrition poor. Chest: enlarged bron- chial glands ? Ab- domen: Tb. ? nodules; spleen +; liver +; enlarged disks (1/20/ 12, 2/21/12); T. 97- 102 F.	Wassermann + 2/24/12	Has had tubercu- lin regularly since admission to date
10	11	F	Poliomyeloneceph- alitis	Negative	Pneumonia; date ? Typhoid date ? Un- able to walk for 2 yrs.	Teeth notched and de- cayed; tonsils +; spastic lower limbs.	Noguchi + 2/9/11	
15	10	F	Lesion of spinal cord 9/30/10	Negative	Weak at birth; mouse at 7 years; varicella at 8 years; full 1 yr. ago; since spinal symptoms.	Nutrition poor; par- otid R. limbs; teeth notched; glands +; patellar +; tonsils and adenoids re- moved; no splenectom found.	Noguchi + 10/5/10	
31	1½	F	Anemia	Negative. Father had 2 negative Wass- ermans.	Normal development. For 3 weeks daily rise of temperature; cause ?	Pale; nose flat; tonsils +; dactylitis.	Noguchi + 1/7/11 Wassermann 1/17/11	Calomel. Tests by different men.
39	2	M	Lobar pneumonia	Negative.	Pneumonia at 1 year.	Nutrition poor; pale; nose flat; vacant stare and "grim"; tonsils +	Wassermann + 2/19/12	Pirquet negative 2/10/12

GROUP IV

3	3	M	Tb. Meningitis 4/4/12	Father had "soft chan- cre" 7 years before; mother had one mis- car.; younger brother died one year ago of "heart trouble"; al- ways delicate.	Gen. development nor- mal; present illness began 7 weeks ago.	Typical meningeal signs; Sp. Fl. clear; lymphocytes; Tb. ba- cilli; Pirquet negat. Double otitis media.	Sp. Fl. Noguchi +++	Died 4/8/12. Au- topsy (on head only) showed tb. meningitis, ba- cilli in exudate at base of brain; no syphilitic changes.
18	1½ 1¼	M	Congenital heart disease 1/4/11  10/27/11	Mother had miscar- riage 5 years ago; 3 other child'n healthy; mother died 1 week ago of pneumonia and endocarditis.	Full term, instruments, condition good. Per- tussis 3 mos. ago fol- lowed by pneumonia. Double otitis, 1 mo.	Nutrition poor; or- ganic heart-signs; ears discharging; weight 10 lbs., 2 oz.	Noguchi + 2/9/11	Left 7/3/11 Mercury from 2/28/11 to 4/6/11
24	7	F	Endopericarditis 7/21/11	Mother had 2 miscar- riages; poor health since last baby, five years ago.	Measles at 11 mos.; scarlet fever at 4 yrs. Sore throat frequent- ly; for 3 weeks ab- dominal pain.	Nutrition poor; pale; tonsils +; pericardi- tis; mitral murmur.	Noguchi + 8/6/11	Blood and Sp. Fl. from autopsy negative, by both Wassermann and Noguchi. No syphilitic changes in tissues
14	8	M	Epilepsy 3/18/11	Epilepsy in maternal G. M. Mother had petit mal; 3 other children well.	Labor instrumental; mentally slow; mea- sles and scarlet fever 4 yrs. ago; varicella 2 mos. ago; pneumonia 3 mos. ago; "spells" for 2 years.	Head asymmetrical; otitis; pigeon-breast.	Noguchi + 3/9/11	
2	12	M	General debility Tb.? 11/14/10	Mother had 3 or 4 mis- carriages; 7 other children well.	Developm't backward; dull mentally; pneu- monia 4 years ago; scarlet fever 2 years ago; measles 2 years ago.	Poor development; glands +.	Noguchi + 11/26/10	Pirquet + 11/26/10

TABLE 4.- (CONTINUED)  
GROUP V

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
1	3	M	Millary Tuberculosis	Uncle died of phthisis	Always delicate; typhoid symptoms 3 weeks.	Emaciation; glands +; spleen +; T. 98-104 F.; blood culture neg. Widal negative.	Noguch +	Pirquet negative left in 1 wk; unimproved.
7	5	F	Tb. Spine 7/15/10	Negative	Portusula at 1 year; present trouble began 1½ years ago.	Spinal deformity; glands +; consolidation R. lung, post. on 1/6/11.	Noguch + 2/1/11	
8	4	F	Tb. Knee	Negative	Development normal; knee symptoms 3 mos.	Pale, nutrition fair; tonsils +.	Wassermann +	Pirquet ++
20	8	M	Endo-pericarditis 3/16/11	Father died phthisis, 2 years ago.	Weak since 5 yrs. old; measles and diphtheria; rheumatism 1 yr. ago; for 1 mo. cough, pain in chest, weakness, dyspnea.	Pale, nutrition fair; tonsils +, glands +. Endo-pericarditis.	Noguch Doubtful 3/29/11 Weakly + 4/6/11 Positive 5/11/11	
12	4	M	Amaurotic family Idiocy 6/24/10	Negative	Always delicate; at 1 week vomiting and convulsions.	Emaciation; eyes show characteristic changes; glands +.	Noguch - 6/26/10 Noguch + 1/22/11	Death 9/8/11
10	3	M	Little's disease	?	Always delicate, measles, date of meningeal symptoms for 2 wks.	Nutrition poor; rigidities; glands +; rick-ets signs.	Noguch 6/5/10 Noguch + 1/19/11	Pneumonia 1/18/11. Antitoxin.

31	1/6	M	Enterocolitis, Convulsions	Negative.	Well at birth; "cold" for 10 days; convul- sions for 24 hours.	Emaciation, pallor; moribund. Sp. Fl. neg. for bacteria; Sp. Fl. pos. for Noguchi.	Blood post-mor- tem gave posi- tive Noguchi	Autopsy 10 hrs. after death; no signs of syphilis.
38	1 1/3	M	Rachitis, gastro- enteritis 6/29/10	Negative.	Negative	Developm't and nutri- tion poor; rachitic signs; spleen +.	Noguchi ++ 11/28/10	Pirquet negative. Died 2/11/11. Autopsy showed no gross nor mi- croscopic signs of syphilis.
33	7	M	Osteomyelitis 3/27/10 Readmitted 12/7/10	Negative	Measles at 1 1/2 years; scarlet fever at 3 1/2 years; for 7 mos. pain in legs, fever, sweat- ing.	Nutrition fair; both tibiae have discharging sinuses. As above.	Noguchi + 12/20/10	Disch'd 9/10/10 improved Given Hg. and KI. Improved.
39	5	F	Still's disease	Negative.	Measles 3 years ago; pertussis 2 years ago; for 1 year pain in limbs and joints; un- able to walk.	Nutrition poor; rachi- tic changes; swelling and stiffness of joints.	Noguchi + 10/24/10 1/9/11 Noguchi — 1/19/11	Hg. and KI. from Oct. to March, 1911.

The patient was taken out of the hospital after a week's stay and nothing further was heard of him. There was nothing about him to suggest syphilis.

Concerning the other cases of the group, there is possibly more ground for considering them as syphilitic; five of them involve disease of the osseous system: two of joint trouble thought to be tuberculous, a chronic osteomyelitis, a case of Still's disease, one of Little's disease with bony changes thought to be rachitic. The tendency of the syphilitic virus to attack the bony tissues is well known, and syphilis cannot with certainty be excluded in any of these cases. Clinical observations and serum tests of the future must determine how frequently these bone affections are due to luetic infection.

The case of endocarditis included in this group is interesting; it showed a reaction at first "doubtful," a week later "faintly positive," and a month later "positive"; in view of these reactions and of the frequency with which the other cases of endocarditis of this series, cases with suggestive or characteristic signs of syphilis, have shown positive reactions, there is probably little doubt of the basic nature of this case, little doubt that it is syphilis. But as the case illustrates a condition "on trial," as it were, in this paper, and presented none of the signs regarded in the past as suggestive of syphilis, it must be classified, for the present, at least, in this group. Studies of the future may or may not show that endocardial affections are of such frequent occurrence in congenital syphilis that their presence is suggestive of the disease and must always arouse a suspicion of its existence.

The third supposition, that the reaction is incorrect and is due to some error in technic, must be considered. Such an error might arise from (1) change in the blood after taking and before testing, or from (2) some imperfection in one of the substances or reagents used. Due care was used in the handling of the blood, keeping it at a proper temperature, etc. It is of course possible that hemolysis may have taken place before testing and thus at the test hemolysis was prevented and a positive reaction obtained. But against this theory is the fact that specimens of blood from other patients at the hospital, obtained at the same time and handled in the same manner, gave in some instances negative reactions, in others positive reactions. Similarly with the various substances used for antigens, amboceptors, etc.; the same materials used in our cases were used at the same time on patients from another hospital and found to be working well, giving positive reactions on known syphilitics, mostly adults, yet negative results on still others undoubtedly not syphilitic. I have taken pains to "check up" with Dr. Nicoll these points by review of the original records on the given dates of each of the cases in Group V. and it is evident that the error, if error there be, is not in the quality of the different substances used. I cannot be so sure of the absence of error



under the first possibility, i. e., some change in the blood used; particularly might this be true with regard to Case 31, when the blood was obtained at autopsy ten hours after death; for Candler and Mann have shown that post-mortem decomposition may alter the reaction whether of the blood or spinal fluid, an ante-mortem positive reaction being converted into a negative, and vice versa.

Taken as a whole, then, Group V may be summarized briefly as follows: There is no ground, except a positive serum reaction, for regarding four of the group, Numbers 1, 12, 20 and 31, as cases of syphilis; there is some ground for regarding the remaining cases as syphilitic, and in them this disease cannot with certainty be excluded. Our third question, then, Does a positive serum reaction, without suggestive physical signs, mean syphilis? must, in the present state of our knowledge, be answered in the negative. Investigations of the future, however, may broaden our conception of the term "suggestive" signs so that it will include signs now not regarded as "suggestive."

#### NEGATIVE CASES

The negative cases require but little further comment. The diagnoses are given in Table 1. The relative frequency of suggestive family history and suggestive physical examination in the two divisions, positive and negative, has already been noted, there being far fewer such records in the negative than in the positive cases. Among the negative ones were only three cases with such marked physical signs that syphilis could not be excluded. The first of these was a 2-months-old baby, of the Mongolian type of idiocy, with a congenital heart lesion, asymmetrical head, flattened nose and "chicken breast." He was the fifth child, the first four pregnancies having resulted in miscarriages. The test (Noguchi) was done with his spinal fluid; possibly his blood would have given a positive result.

The second suspicious, yet negative, case was a younger brother of patient, Case 17. He was much below par, with bony changes regarded as rachitic, and with a well-marked syphilitic family history (Table 3, Case 17).

The third case was a 12-year-old girl, of backward development, with marked keratitis and suspicious looking teeth.

#### RÉSUMÉ

Surveying now as a whole this series of 101 hospital children who have been tested by the Wassermann serum reaction, certain facts strike us.

First, we are impressed with the large number of cases presenting a positive reaction, 38 per cent., over a third, giving such a result. The most of these, as we have seen, we are justified in regarding as syphilis; all, in fact, except the patients in Group V. Deducting the ten cases

forming this group, we have twenty-nine (28 per cent.) cases of syphilis among the first hundred children, selected mostly at random, in one of our large American hospitals; that is, nearly one out of every three patients. It has been difficult in the past to obtain an accurate idea of the prevalence of congenital syphilis. That syphilis in general is a lamentably wide-spread disease is well known. Erb, for example, found that out of 10,000 cases of all varieties of disease in his practice, 21 per cent. had syphilis. He believes that 12 per cent. of the adult population of Berlin has syphilis. This means, eventually, a large amount of the congenital form of the disease. Yet it is not generally regarded as being common. Beekel, for example, examined the record of the Babies' Dispensary in Cleveland and found only forty-five cases among 3,500 patients, about 1.33 per cent.; these were all clinical cases and before the days of the serum test.

The observations made in this paper, based on clinical examination and the serum test, would tend to show, however, that there is a large amount of congenital syphilis among hospital patients.

Next we are struck with the great variety of conditions in which we find a positive serum reaction, corresponding with the protean character of syphilis. The greatest number of positive reactions is found, furthermore, in the bony, nervous and circulatory systems, tissues, it will be recalled, particularly apt to be attacked by the syphilitic virus.

The comparatively large number of positive cases without physical signs, the "symptomless" children, is another striking phenomenon, fourteen of the cases (37 per cent.) being so lacking. This again is quite in keeping with the character of congenital syphilis, at least of the late variety, and emphasizes the difficulty of arriving at a diagnosis, and the importance of the serum test in unearthing these obscure cases.

The number of cases reported in this series is, however, small, and it may be that analysis of larger numbers of cases will modify the points which have been discussed, and that the figures obtained in the first hundred cases may be considerably altered by future studies. Enough has been set forth, however, to demonstrate the importance of the serum test in studying our anemic, maldeveloped children and the desirability of applying this test on a large scale to these children, in order, first, to determine to what extent syphilis prevails among them, and, secondly, to institute proper treatment.

The subject is, to my mind, an important one, a broad one; important not only to the victims of the disease itself, but also to the community at large and for the future welfare of the race. If congenital syphilis is nearly as prevalent among certain classes of the community as the studies in this paper would seem to indicate, it is a matter of grave concern to all, especially to us as pediatricians, on whom must devolve the responsibility of determining the extent of the evil and its proper management. We

have had put into our hands recently, in the Wassermann serum test, a method of investigation which, together with careful, painstaking clinical observations on a large scale, will give us accurate information, as never before, concerning a malady notoriously fatal in extreme infancy, lamentably blighting in later childhood. But the use of this new weapon must be wide-spread, must be carried out in large numbers of patients before we can answer finally the questions propounded in this paper and the various points suggested by those questions.

This study is therefore offered, not by any means as a final solution of the questions, but rather as a preliminary report, and with the hope that others will also take up and carry on the work.

I am indebted to my fellow members of the Hospital staff for permission to study the children in their wards. I am also greatly indebted to Drs. E. R. LeCount and J. H. Hewitt for the reports on the autopsies.

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## REFERENCES

- Beekel: *Ohio State Med. Jour.*, 1910, vi, 490.  
Candler and Mann: *British Med. Jour.*, 1912, No. 2671, p. 537.  
Dean: *Lancet*, London, 1910, clxxix, 227.  
Erb: (Quoted by Ravold), *Ill. Med. Jour.*, 1911, xix, 269.  
Hochsinger: *Wien. klin. Wehnschr.*, 1910, xxiii, 881, 932.  
Hugel and Ruete: *München. med. Wehnschr.*, 1910, ii, 79.  
Kaliski: *Arch. Int. Med.*, 1910, vi, 205.  
Knöpfelmacher and Schwalbe: *Ztschr. f. Kinderh.*, 1912, iii, 428.  
Mulzer and Michaelis: *Berl. klin. Wehnschr.*, 1910, xlvii, No. 30, 1403.  
Noguchi: *Serum Diagnosis of Syphilis*, Ed. 2, 1911.  
Stroscher: *Dermatol. Ztschr.*, 1910, xvii, 485.  
Warthin: *Am. Jour. Med. Sc.*, 1911, cxli, 398; *Jour. Am. Med. Assn.*, 1912, lviii, 689.

## ACUTE DUODENAL INDIGESTION IN CHILDREN \*

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The relation between the physiology of digestion and the diseases of the gastro-intestinal canal has received considerable attention in recent years and has thrown much light on many obscure digestive disturbances. A large part of our knowledge about bile and the effects of obstruction to the flow of the bile, comes from animal experiments and there is only a relatively small amount of literature on the physiology and pathology of bile which has been applied to infancy and childhood. A résumé of these facts is necessary because they explain much that, otherwise, is obscure in the treatment of acute duodenal indigestion, and give a physiologic foundation for our conception of the pathologic processes to be studied. They naturally divide themselves into physiology of bile, biochemistry of bile and its products of decomposition, and the action of bile during digestion.

### PHYSIOLOGY

Bile varies not only in amount, but also as regards its composition, as is shown by the accompanying table.<sup>1</sup>

TABLE SHOWING COMPOSITION OF BILE FROM THE LIVER AND FROM THE GALL-BLADDER

	Liver-Bile	From Gall-Bladder
Solids .....	2.06	16.02
Water .....	97.94	83.98
Mucin and pigments.....	0.28	4.44
Alkali bile-salts .....	0.85	8.72
Taurocholates .....	0.11	1.93
Glycocholates .....	0.74	6.79
Fatty acids from soaps .....	....	1.06
Cholesterol .....	0.08	0.87
Lecithin .....	....	0.14
Fats .....	0.03	0.15
Soluble salts .....	0.80	0.30
Insoluble salts .....	0.02	0.24

Bile pigments and salts find their way into the intestine very early in the third month of fetal life.<sup>2</sup> This bile, together with the secretion

\*Obstructive jaundice, the terminology used in this paper, is that adopted by the Department of Pediatrics of the Harvard Medical School.

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1. Hammarsten, Olaf: *Nova acta Reg. Soc. Upsal, Serie III.* 1894; quoted in *Abderhalden-Hall: Text-book of Physiological Chemistry*, New York, 1908, p. 517.

18. The attempt was also made to determine whether the patient's blood condition, 1904, p. 319.

of the rest of the canal and some desquamated epithelium, accumulates to form the meconium. After birth the cycle of a normal digestion starts and from then on is elaborated until it reaches the adult type of digestion. The intestinal canal is sterile at birth, but shortly afterwards it becomes infected and remains so for the rest of life. The type of bacteria inhabiting the canal depends on the kind of food which surrounds them. They tend to belong to the acid-forming group while the baby is fed with human milk, and to the putrefactive- or alkali-forming group when the food is cow's milk.<sup>3</sup> This fact has a bearing on the chemical changes which bile undergoes after it enters the intestinal canal. Bile is excreted from the liver in the form of bilirubin and is changed through oxidation and bacterial action into biliverdin and later hydrobilirubin. This in its turn may be converted into leukohydrobilirubin, when decomposition is more intense. A considerable part of the bile which has already performed its part in digestion is absorbed and carried back to the liver to be reconverted into bilirubin. Hydrobilirubin does not appear in appreciable amounts in the feces until putrefaction is well established. This commences when a baby begins to take cow's milk, which contains larger quantities of casein than human milk and thus gives a suitable food for the proteolytes, or putrefactive group of bacteria, to grow on. There are two bodies, urobilin and urobilinogen, which correspond with hydrobilirubin and leukohydrobilirubin but which are not chemically identical with these bodies. It has been proved that urobilinogen cannot be formed without the action of bacteria and so it is impossible to obtain Ehrlich's "aldehyde" test for urobilinogen in either the urine or the feces when bile is blocked from the intestines. This body is of enough importance in the consideration of acute duodenal indigestion to warrant a detailed description of it.

#### UROBILINOGEN

In 1901 Ehrlich<sup>4</sup> observed that an acid solution of dimethylaminobenzaldehyd caused a cherry-red color to appear in urine, which became much more intense in many pathologic conditions. There was considerable discussion about the significance of this reaction until O. Neubauer<sup>5</sup> established the fact that it is a test for urobilinogen. It is easily oxidized into urobilin when exposed to air and light.<sup>6</sup>

3. Kendall: Observations on Aciduric Bacteria, *Jour. Med. Research*, 1910, N. S., xvii, 153.

4. Ehrlich: Ueber die Dimethylamidobenzaldehydreaction, *Med. Wehnschr.*, Berl., 1901, ii, 151.

5. Neubauer: Ueber die neue Ehrlichsche Reaction mit Dimethylaminobenzaldehyd. *Sitzungsbericht der Gesellsch. f. Morph. u. Phys. in München*, 1903. Reported in *München. med. Wehnschr.*, 1903, I, No. 2, p. 1846.

6. Salliet: De L'Urobiline dans les urines normales, *Rev. de méd.*, 1897, xvii, 109.

Bookman<sup>7</sup> and Langstein<sup>8</sup> summarize the knowledge of the subject and incidentally mention results which correspond with my observations on its action during occlusion of the bile ducts. The decomposition of bile takes place mostly in the large intestine where bacterial action is most pronounced. Herter<sup>9</sup> showed that Ehrlich's "aldehyde" reaction could be augmented by skatol and also intensified by a diet rich in meat. He was also able to cause the reaction to disappear from the urine of dogs when he gave them a milk instead of a meat diet. This latter observation was probably due to the change in bacterial action and a lessened decomposition, because I have found the reaction repeatedly in the urine of babies fed on mixtures of cow's milk only. Urobilinogen is only present in the urine when bile flows into the intestinal canal and is always absent when there is occlusion of bile. The test is performed in the following way:

Add a few drops of Ehrlich's reagent (2 per cent dimethylaminobenzaldehyd in 5 per cent. HCl) to 5 c.c. of unheated urine. There is no change of color. Then gently warm the urine and if urobilinogen is present in normal amounts it will turn a delicate cherry-red color. This can be best seen by looking down through the depth of the test tube. If urobilinogen is present in abnormal amounts, the urine turns distinctly cherry-red on adding the reagent in the cold. When urobilinogen is absent, the cherry-red color cannot be obtained even after heat is applied.

#### THE RELATION OF BILE TO THE DIGESTION AND ABSORPTION OF FAT

Bile has the property of activating the pancreatic proferment steapsinogen into steapsin.<sup>10</sup> The absence of bile, however, does not stop the action of steapsin when it is once secreted; without it the fats may be split in part, but they are imperfectly absorbed.<sup>11</sup> The action of bile on fat during digestion is not simple and the changes which fat undergoes must be briefly enumerated before it can be discussed. The greater portion of the fat in cow's milk is in the form of neutral fat. During digestion neutral fat is first split into fatty acids, which in turn are

7. Bookman: Die physiologische Bedeutung und der klinische Wert der Ehrlichschen Dimethylaminobenzaldehyd reaktion im Kindesalter. *Jahrb. f. Kinderh.* N. F., 1906, lxiv, 206.

8. Langstein: Ein Beitrag zur Kenntnis des weissen Säuglingsstuhls, *Festschrift für Salkowski*.

9. Herter: Ehrlich's Aldehyd Reaction in the Urine. *Jour. Biol. Chem.*, 1908, iv, 403.

10. Nencki: Ueber die Spaltung der Säureester der Fettreihe und der aromatischen Verbindungen im Organismus durch das Pankreas. *Arch. f. exper. Path. u. Pharm.*, 1886, xx, 367.

11. Schwann: Versuche um auszumitteln ob die Galle im Organismus einer für das Leben wesentliche Rolle spielt. *Müller's Arch. f. Anat. Physiol. u. wissenschaft. Med.*, 1844, 127; Dastre: Recherches sur la bile. *Arch. phys. norm. et path.* 1890, 5 S., ii, 315.

converted into soaps. Pflüger's<sup>12</sup> investigations led him to the conclusion that unsplit fat cannot be absorbed. There is much evidence which warrants the statement that the stage of soap formation is necessary for the most efficient absorption of fat.<sup>13</sup> The emulsification of fats is favored by the presence of bile, which also increases the fat-splitting action of the pancreatic juices eight times or more.<sup>14</sup> It has been proved that the cholic acid component of the bile salts is responsible for the rapid digestion of fats.<sup>15</sup> Bile has the property of dissolving fatty acids,<sup>16</sup> of increasing the solubility of soaps in water, and of preventing the gelatinization of soaps.<sup>17</sup> Its action on soaps is probably of more importance than its action on fatty acids. When bile is occluded from the intestinal canal, absorption of fat is interfered with and metabolism is abnormal.

#### THE EFFECT OF OBSTRUCTION OF BILE ON THE METABOLISM

Most of the knowledge on this subject comes from animal experiments, but there are a few experiments on man. Fr. Müller's<sup>18</sup> and Riecke's<sup>19</sup> experiments on adults with occlusion of the bile ducts, showed that there was no abnormal loss of nitrogen, while R. Schmidt<sup>20</sup> found an enormous loss of nitrogen in a patient with catarrhal jaundice plus anorexia, who was very much underfed. The conclusion may be drawn from these experiments that there is no loss of nitrogen during the disease unless anorexia becomes pronounced and is accompanied by starvation. The digestion of carbohydrates also progresses in a normal manner. Experimentally, the absorption of fat is seriously interfered with; only 40 per cent. of the fat ingested is absorbed instead of the normal 90 per cent. Rohmann<sup>21</sup> and Fr. Müller<sup>18</sup> have shown that the same relation holds good in man. In obstruction to bile, the fat content

12. Pflüger's *Arch. f. d. ges. Physiol.*, 1900, lxxx, 111; 1900, lxxxi, 385; 1900, lxxxii, 303; 1901, lxxxv, 1; 1901, lxxxviii, 299; 1902, lxxxix, 281; 1902, xc, 1.

13. Talbot: See review of literature in *Physiology and Pathology of the Digestion of Fat in Infancy*. *Am. Jour. Dis. Child.*, 1911, i, 173.

14. Hewlett: *Effect of Bile upon the Ester-Splitting Action of Pancreatic Juice*. *Bull. Johns Hopkins Hosp.*, 1905, xvi, 20.

15. Fürth and Schutz: *Ueber die Bedeutung der Gallensäure für die Fettverdauung*. *Zentralbl. f. Physiol.*, 1906, xx, 47.

16. Moore and Rockwood: *On the Mode of Absorption of Fats*. *Jour. Physiol.*, 1897, xxi, 58.

17. Moore, Rockwood and Parker, quoted from von Noorden, *Metabolism and Practical Medicine*, Chicago, 1907, ii.

18. Müller: *Untersuchungen über Ikterus*. *Ztschr. f. klin. Med.*, 1887, xii, 45.

19. Riecke: *Harnstoff, Ammon, u. Phosphorsäuregehalt Leberkranker*. *Diss. Würzburg*, 1886; quoted from von Noorden, *Metabolism and Practical Medicine*, Chicago, 1907, ii, 236.

20. Schmidt: *Zur Stoffwechselfath. des Ikterus catarrhalis u. zur Frage der Paracholie*. *Zentralbl. f. inn. Med.*, 1898, xix, 113.

21. Rohmann: *Beobachtungen an Hunden mit Gallenstiel*. *Pflüger's Arch. f. d. ges. Physiol.*, 1882, xxix, 509.

of the feces is more than double the normal, while 55 per cent. of the fat in the food, instead of 8 to 12 per cent. as in health, is lost in the feces. Schmidt<sup>22</sup> found in adults that 21.45 per cent. to 26.61 per cent. of the dried feces of healthy individuals is fat and that this fat represented 5.16 per cent. to 5.91 per cent. of the fat ingested. In closure of the bile duct he found that 43.87 per cent. to 53.59 per cent. of the dried feces was fat and that 22.79 per cent. to 27.70 per cent. of the fat ingested was lost in the feces. Gaultier<sup>23</sup> found an absorption of only 37 per cent. to 53 per cent. of the fat in the food. These estimations of fat in the stool were not done by the newer method of Kumagawa and Suto,<sup>24</sup> which might have shown larger losses of fat, as it gives higher figures than the older methods. The clay color of the stools is caused partly by the absence of bile pigments and partly by the presence of excessive quantities of fat. It must be remembered, in this connection, that leukohydrobilirubin is white bile and that the white stools, such as are seen in other types of indigestion due to fat, do not mean of themselves that there is no bile in the feces.

Bile has no effect on the digestion of sugar, but it has been known for a long time that sugars have an unfavorable influence on patients with acute duodenal indigestion. A possible explanation of this fact is that excessive amounts of sugar may supply a media of growth for the normal fermentative bacteria of the upper gastro-intestinal canal. These bacteria may overgrow in suitable surroundings to such an extent that as a result of their activities a secondary irritation of the duodenal mucosa is set up. This theory is based on the assumption that bacteria of the fermentative group are present to act on the sugar. Starch, on the other hand, is broken down slowly into sugars so that only a small amount of sugar is set free at a time. Thus, in the first instance, a flood of sugar stimulates the bacteria to intense activity, while in the second, there is only a dribble which is absorbed before it can effect the bacteria.

*Acute duodenal indigestion* is a relatively common disease. During the past year there have been twenty-four cases in the Children's Medical Out-Patient Department of the Massachusetts General Hospital, which I was able to study with more or less care. The onset of the disease varies; it may be sudden with fever, vomiting, pain in the stomach which

22. Schmidt: Schmidt and Strasburger. Die Fäzes des Menschen. 3 Aufl. Berlin, 1910, 153.

23. Gaultier: Essai de coprologie clinique de l'exploration fonctionnelle de l'intestin par l'analyse qualitative des graisses dans les feces. Presse méd., 1904, xii, 612.

24. Kumagawa and Suto: Ein neues Verfahren zur quantitativen Bestimmung des Fettes und der unverseifbaren Substanzen im tierischen Material nebst der Kritik einiger gebräuchlichen Methoden. Biochem. Ztschr., 1908, viii, 212.



lasts one or two days and is followed by jaundice, clay colored movements, bile in the urine and loss of appetite; or insidious, without fever, following some indiscretion in diet, more especially fats or sugars. Stooss<sup>25</sup> reports a family of children in which jaundice was brought on by a honey cure prescribed by the father. Large and small epidemics of jaundice have been reported.<sup>26</sup> Apparent contagion was traced from one sister to the other in two of my cases. These cases of infectious jaundice were clinically identical with most of the cases studied by me, but did not run the severe course described in Weil's disease. All but two of seventy cases which were seen in the out-patient department of the Massachusetts General Hospital since 1903 occurred between the first of September and the middle of January.

#### CASE REPORT

The following case illustrates the various points brought out in the discussion of the disease:

Herbert C. (M.G.H., O.P.D. 166,473) was first seen Feb. 20, 1911. He was 10 years old. His family history and past history were unimportant. He was well up to six weeks previously, when he complained that his stomach was hurting him. At the time he was eating ten to twelve raw apples a day. About two weeks ago he became feverish, and complained of headache; seven to eight days ago he became quite yellow and the fever disappeared. He noticed that his stomach was swollen but did not see that his urine and stools were abnormal until five days ago when the jaundice became more marked and the family physician was called in. The stools on examination were found to be lead- to clay-colored and the urine was very dark.

The physical examination showed very marked icterus of skin, soft palate and conjunctivæ. The pupils were equal and reacted to light. The mouth, throat, heart, lungs and abdomen were normal. The liver dulness extended from the upper border of the fourth rib to 4 cm. below the edge of the ribs in the nipple line, where the edge was easily felt; it was not tender. The spleen was not palpable. The urine contained large quantities of bile and showed no test for urobilinogen. This meant that there was no bile flowing into the digestive tract.

Treatment consisted in restricting his diet to meats, starches and skimmed milk, fats and sugars being excluded as far as possible. Three days later, February 23, he was again seen and reported that he was much better. The jaundice was less marked and although the urine still contained bile (bilirubin), it also showed a large excess of urobilinogen. This meant that bile was entering the intestinal canal. The stool was gray, formed, shiny, of foul odor; it showed under the microscope no meat fibers or starch granules, but there was a large excess of fat in the form of soaps.<sup>27</sup> Four days later, February 27, he reported that he was getting along splendidly, that the urine was of more normal color, and that the day previous the stool looked more natural. The urine contained less bile (tincture of iodine test) and still had an excess of urobilinogen. The stool was

25. Stooss: Pfaundler and Schlossmann: Diseases of Children. Philadelphia and London, 1908, iii, 269.

26. Stooss: *Loc. cit.*, note 25; Vaisey: An Epidemic of Infectious Jaundice. Brit. Med. Jour., 1911, i, 935; Hallows: An Epidemic of Infectious Jaundice. Brit. Med. Jour., 1911, i, 1464.

27. The methods used in examining the stools were reported by me in Arch. Pediat., February, 1911.

light yellow, smooth and macroscopically perfectly digested. Under the microscope it showed a small excess of fat in the form of soaps. The flow of bile into the intestinal canal was therefore nearly normal. On March 3 he reported that the stools were brown and constipated and the urine almost normal. On examination he was very slightly jaundiced, the liver had diminished in size, extended from the sixth rib to just below the costal margin in the nipple line. He looked better in every way and had gained 5 pounds in twelve days on the restricted diet. The urine showed a slightest possible trace of bile by the iodine test and a large excess of urobilinogen. The stool was still light yellow, smooth and of foul odor. Under the microscope it showed a small amount of fat in the form of soaps.

The analysis of the cases studied brought out several interesting facts: The disease came as a complication of such infections as otitis media, diphtheria, and the exanthemata in 15 per cent. of the cases. The onset was sudden with fever and vomiting in 75 per cent., and therefore suggested an infectious origin; the liver was enlarged in 74 per cent., and tender in 13 per cent.; the spleen was not felt in any case. Urobilinogen was absent from the urine in every case where there was complete obstruction to bile and was found in excessive amounts when the obstruction was removed. The stools were recorded as white in 36 per cent., creamy in 14 per cent., and clay colored in 50 per cent. of the cases during obstruction, and, under the microscope, always showed an excess of fat which was entirely in the form of soaps, while there was constipation, and as both fatty acids and soaps when there was diarrhea. In one instance in which the diet was particularly bad, there was also an excess of starch, but in all other cases starch and meat were perfectly digested.

When there is complete obstruction to the common duct, bile in the form of bilirubin is dammed back into the circulation, colors the tissues and part overflows in the urine. Urobilinogen cannot be found in the urine because bacterial action on bile is necessary for its formation; this of course only takes place in the intestinal canal. As a result, the fat in the food is digested and absorbed only in part, and there is a clay-colored alcoholic stool which is composed almost entirely of fat. In the majority of my cases this fat was in the form of soaps. In some instances there is constipation and in others a diarrhea of putrid, rancid stools containing fine mucus. The diarrhea is a result of prolonged irritation of the intestinal mucous membrane, due to the stagnation and decomposition of fat, which is brought about by the action of the intestinal juices and bacteria, thus complicating the duodenal indigestion with a secondary intestinal indigestion. When the bile flows again into the intestine the fat quickly disappears from the stool and abnormal quantities of urobilinogen appear in the urine. On the basis of these findings two explanations may be given: Either the excessive amounts of urobilinogen are due to excessive putrefaction accompanying the disease,

plus a diet containing a large amount of meat, or acute duodenal indigestion is not a simple blocking of the common duct by mucus. It is conceivable that the agent which caused the plug of mucus to form in the common duct may have extended up into the small bile capillaries of the liver. In that case, the liver cells could not act normally and urobilinogen would not be converted back into bilirubin in the normal manner; this would result in an obstruction in the liver, which would cause urobilinogen to back up and overflow in excessive amounts in the urine. Münzer and Block<sup>28</sup> conclude as a result of their experiments that increased amounts of urobilinogen in the urine always means disease of the liver cells to a greater or less degree.

#### TREATMENT

Metabolism experiments and an understanding of the physiology of bile makes it obvious that fat and sugars should be excluded from the diet. Conversely proteins, especially meat, fat-free milk, or skimmed milk, and thoroughly cooked simple starches (potato is the least digestible) may be safely given. Fortunately, the disease is of relatively short duration, because a fat-free diet could not supply the requisite number of calories to sustain health indefinitely. The appetite is always poor and can be best stimulated by tincture of *nux vomica*, in doses corresponding to the age of the patient. Mucus is the natural protective agent of the gastro-intestinal canal and is thrown out by the mucous membrane whenever there is any form of irritant present. We know that mucus is soluble in alkalies and precipitated by acids, therefore, the mucus plug in the bile duct may be best reached by large doses of alkalies (for example bicarbonate of soda).

The prognosis is always good for life, but recurrences are not infrequent; our knowledge of the pathologic anatomy is, therefore, very scanty. Much work must be done by the pathologist before we can know whether acute duodenal indigestion is a purely local disease or one in which the liver tissue itself is involved.

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28. Münzer and Block: Ueber den Nachweis des Urobilinogens und des Urobilins und die klinische Bedeutung dieser Körper. *Arch. f. Verdauungsk.*, 1911, xvii, 260.

## RÉSUMÉ ON INFECTIOUS DISEASES

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CHICAGO

### ANIMAL EXPERIMENTATION IN SCARLET FEVER

During the past year animal experimentation in scarlet fever has brought out certain facts which may lead us to a solid etiologic basis. Bernhardt<sup>1</sup> reports some interesting experimental work on the transmission of scarlet fever to various forms of monkeys (*Macacus rhesus*, *Macacus cynomolgus*, *Cercopithecus griseus fuliginosus*). The coating was removed from the tongue of a child in the early stages of the disease before the appearance of the so-called "strawberry tongue," and mixed thoroughly with normal salt solution by shaking for an hour. He injected subcutaneously 4 c.c. of this emulsion into the groin of a monkey, and part he rubbed into the mucous membrane of the mouth, tongue and tonsils. After a few days there was a rise of temperature and swelling of the inguinal glands, and on the fifth day the animal showed well-marked symptoms similar to those seen in man, namely, an erythematous exanthem, elevation of temperature, swollen lymph-nodes and scarlatinal tongue. The swollen nodes were removed and treated in the same manner as the coating from the tongue, and the emulsion was injected into another monkey. In this manner he was able to transmit the disease through three different monkeys; but the fourth showed no reaction.

In some of the lymph-nodes streptococci were present, while in others they could not be found. The presence or absence of streptococci did not affect the experiments in the slightest degree. The material injected was sterile in cultures and produced no disturbances when injected into mice.

Control inoculations with streptococci caused no reactions.

Bernhardt concludes that there is a virus present in the coating of the tongue, in the lymph vessels of the skin and in the lymph-nodes. This virus will produce in monkeys certain symptoms which are practically identical with those of scarlet fever in man. That the virus is filterable he proved by obtaining the scarlatinal symptoms in two cases with material that was previously passed through a bacteria filter.

Landsteiner, Levaditi and Prasek,<sup>2</sup> working along the same line as Bernhardt, transmitted a similar chain of scarlet fever symptoms to chimpanzees. With the lower forms of monkeys used by Bernhardt they were not successful.

1. Bernhardt: Deutsch. med. Wchnschr., April 27, 1911, p. 791.

2. Landsteiner, Levaditi and Prasek: Ann. de l'Inst. Pasteur, October, 1911. p. 754.

The symptoms in chimpanzees were similar to those in man, and a necropsy on one of them showed skin and kidney lesions resembling those found in human beings. Subcutaneous injections of streptococci isolated from one of their cases caused only a local abscess, while an intravenous injection produced no symptoms whatsoever.

Their research corroborates the conclusion of Bernhardt that the virus is filterable, and that the streptococci play at the most a secondary part.

#### BACTERIOLOGY OF SCARLET FEVER

*Streptococcus*.—Schleissner<sup>3</sup> reports the results of extensive investigation in 108 cases of scarlet fever, with special reference to the presence and rôle of the streptococcus. In sixty of the cases (55 per cent.) the streptococcus was found in the blood culture, while in forty-eight cases it was absent in spite of repeated examinations. He found no connection between a positive blood culture and the prognosis; 31 per cent. of the children showing the streptococcus and 35 per cent. of those not showing it had complications. The presence of the streptococcus did not appear to affect the temperature curve. Notwithstanding these negative results Schleissner believes that the streptococcus plays more than a secondary rôle.

*Bacillus*.—Vipond<sup>4</sup> isolated from the lymph-nodes of seven typical cases of scarlet fever a large bacillus with rounded ends, which he considers specific for the disease. It grows readily on the ordinary culture media, and on injection into monkeys produces symptoms similar to those obtained by Bernhardt with his filterable virus from the lymph-nodes of monkeys.

Koessler and Koessler,<sup>5</sup> after numerous serum experiments, conclude that (1) the serum of scarlet fever patients contains specific antibodies for an unknown virus; (2) this unknown virus is present especially in the cervical lymph-nodes.

#### HYPEREMIA TEST IN SCARLET FEVER

Leede<sup>6</sup> reports the results of his observations concerning the diagnostic test for scarlet fever originated by Rumpel in 1909. Passive hyperemia is produced by a broad rubber constrictor placed on the arm above the elbow joint, care being taken not to obstruct the arterial flow. After ten or fifteen minutes the band is loosened. The skin over the flexor surface of the elbow joint is then stretched until it appears anemic, and if the reaction is positive, petechiæ are readily visible. Leede attributes the phenomenon to changes in the walls of the capillaries.

3. Schleissner: *Ztschr. f. Kinderh.*, 1911, Orig. iii, 28.

4. Vipond: *Arch. Pediatrics*, xxviii, 1911, p. 564; *Canad. Med. Assn. Jour.*, November, 1911, p. 329.

5. Koessler and Koessler: *Jour. Infect. Dis.*, Nov. 9, 1911.

6. Leede: *München. med. Wchnschr.*, 1911, lviii, 293 and 1673.

In 200 cases of scarlet fever the sign was absent only once, and that was in an extremely fat girl. The sign can usually be elicited several weeks after the onset, and in one case, complicated by nephritis, was present after 104 days.

Strauch<sup>7</sup> employed this test in 340 cases, including sick and well of all ages. It was present in about half of 160 individuals in health (45 per cent.). Girls showed much less tendency to react than boys. Of 180 sick persons, 107 were positive (56 per cent.). The scarlet fever (twenty-three), and the measles cases (thirteen) all reacted. It was present in various percentages in many other diseases, and in 100 per cent. of blood diseases. Mayr<sup>8</sup> found the phenomenon in twenty out of 100 cases of skin and venereal diseases. Leede in a later communication states that he did not claim that the sign is pathognomonic, but that it is the most constant symptom in scarlet fever and therefore is of great negative value. Leede tested the sign in certain blood diseases without reaction, contrary to the findings of Strauch.

Pastia<sup>9</sup> describes a linear erythematous exanthem which is localized on the flexor surface of the elbow joint. The phenomenon appears at the same time as the rash appears and remains as a linear pigmentation after the rash has disappeared. He believes that the sign will bear the same relation to scarlet fever that Koplik spots do to measles.

#### THE DIAZO REACTION IN SCARLET FEVER

Woody and Kolmer,<sup>10</sup> guided by the results of the study of the diazo reaction in 502 cases of scarlet fever, conclude that its value is very slight in differentiating scarlet fever from serum disease, because of the comparatively low and inconstant percentage of positive reactions in both of these diseases. It was positive in 17.3 per cent. of scarlet fever and 12.9 per cent. of diphtheria cases in the first week. They found it in 10.8 per cent. of the cases of serum disease, some of which may have been due to diphtheria. These results are contrary to those of Ker, who previously found the reaction negative in serum disease.

#### MENINGEAL SYMPTOMS IN SCARLET FEVER

Sachs<sup>11</sup> reports a series of 400 cases of scarlet fever, sixteen of which showed meningeal symptoms without increased intraspinal pressure — the condition known as meningismus.

7. Strauch: München. med. Wehnschr., 1911, lviii, 1761.

8. Mayr: München. med. Wehnschr., 1911, lviii, 1359.

9. Pastia: Arch. de méd. d. enf., February, 1911, p. 14.

10. Woody and Kolmer: Arch. Pediat., January, 1912.

11. Sachs: Jahrb. f. Kinderh., lxxxiii, (Supplement).

## LUMBAR PUNCTURE IN UREMIA FOLLOWING SCARLET FEVER

Allaria<sup>12</sup> and Sheffield<sup>13</sup> each report a case of uremic coma following scarlatinal nephritis, both of which recovered almost immediately following lumbar puncture. Sheffield believes that a hypodermic of morphin (0.004) and atropin (0.0001) aided in the recovery of his patient.

## THYROID IN SCARLET FEVER

Bauer<sup>14</sup> reports three cases of thyroiditis, without serious symptoms, occurring from eleven to forty-six days after the onset.

## DIABETES FOLLOWING SCARLET FEVER

Brice<sup>15</sup> reports a case of rapidly fatal diabetes developing seven weeks after the onset of a mild scarlet fever.

## PROPHYLAXIS IN SCARLET FEVER

*Vaccine.*—Roszkowski and Czarkowski<sup>16</sup> in seventy-nine cases employed vaccine, prepared from an attenuated culture of scarlatinal streptococci, as a prophylactic measure, with marked success. They divide their cases into three groups; all were vaccinated.

Group I, thirty-three children, not isolated. Three developed a mild scarlet fever, while among unvaccinated relatives, one death and two severe cases developed.

Group II, eleven patients, isolated. No cases developed.

Group III, thirty-five girls in an institution in which there were three severe cases at time of vaccination. No cases developed.

## DIPHTHERIA ANTITOXIN AS A PROPHYLAXIS IN SCARLET FEVER

Benjamin and Witzinger<sup>17</sup> believe that the injection of diphtheria antitoxin has an attenuating effect on an ensuing scarlet fever. Their observations cover 138 cases of scarlet fever which had received diphtheria antitoxin before scarlet fever symptoms had developed. The fever lasted only one day in 76.2 per cent. of the cases, two days in 4.8 per cent. and over three days in 19 per cent. in those cases which had had antitoxin. In those cases which had received no injections the figures are 8.5 per cent., 16.4 per cent., and 75 per cent., respectively.

The investigators believe that the antitoxin is of prophylactic value and suggest the injection of serums of different origins to prolong the period of efficiency of the serums.

12. Allaria: *Gaz. d. osp.*, 1911, xxxii, p. 1291.

13. Sheffield: *Zentralbl. f. Kinderh.*, 1911, xvi, 169.

14. Bauer: *Monatschr. f. Kinderh.*, 1911, ix, p. 560.

15. Brice: *Midland Med. Jour.*, 1911, x, 180.

16. Roszkowski and Czarkowski: *Przegląd Pedyatryczny*, 1911, iii, Abstr. in *Ztschr. f. Kinderh.*, 1911, i, 7, 608.

17. Benjamin and Witzinger: *Ztschr. f. Kinderh.*, 1911, Orig. ii, 123.

In a paper before the New York Academy of Medicine J. A. Kolmer<sup>18</sup> gave the results of his investigations on the glands in twenty-six cases of scarlet fever. He failed to find any organisms resembling those described by Vipond. Confident that scarlet fever streptococci did not possess any specific cultural or morphologic characteristics, he began to study the antibodies of a number of different cultures from various sources, with two main objects in view:

1. To gain, if possible, by such a study, a more accurate knowledge of the relation of streptococci to scarlet fever.
2. To determine if the prophylactic injections of streptococcus bacterins (vaccines) as practiced in Russia could be supported by laboratory investigation.

His investigations led to the following deductions:

1. A streptococcus produced a specific antibody up to a certain limit. The specific nature of these antibodies was seen by complement-fixation reactions in high dilutions between a streptococcus-immune serum and its antigen. With low dilutions the specific nature of the antibody was not brought out.

2. Not only did scarlet fever streptococci tend to produce their own specific immune serum, but likewise the streptococcus causing septicemia and that causing non-scarlatinal angina, etc., tended to produce their own immune serums. Therefore it did not seem any more justifiable to claim a specific streptococcus for scarlet fever than a specific streptococcus for septicemia and other conditions.

3. Finding but 11.2 per cent. positive reactions in scarlet fever tended to show that streptococcus infection in scarlet fever severe enough to produce immune bodies was not so common as generally believed.

One of the three toxic or malignant cases yielded a positive reaction. These severe cases were frequently due to an overwhelming effect of the true scarlet fever virus, without secondary streptococcus infection.

Since it has practically been proved that streptococci are not the cause of scarlet fever, it is difficult, according to Kolmer, to believe that immunization with streptococci can prevent the disease. Such immunizations might be valuable, he believes, in preventing the secondary streptococcal infections which occur in 11 per cent. of the cases of scarlet fever. His studies led to the following conclusions:

1. It is possible to raise the streptococci-opsonic index by the injection of organisms killed by an exposure to 60 C. for an hour.
2. The increase in the quantity of opsonin after three injections is so slight as to make the likelihood of establishing immunity against streptococcal infection dubious.

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18. J. A. Kolmer: Tr. New York Acad. Med., reported in Jour. Am. Med. Assn. Dec. 9, 1911, p. 1942, and in Arch. Pediat., December, 1911, p. 1005.



3. The opsonins are more or less specific toward the strains used in the process of immunization.

He further concluded that:

1. Streptococcus agglutinins are produced slowly by experimental immunization and the quantity is quite variable.

2. These agglutinins are apparently non-specific in character and of no value in differentiating streptococci.

3. They are demonstrable in 12.5 per cent. of scarlet fever patients but only in a comparatively low dilution of serum.

4. There is no relation between agglutinins and complement-fixation antibodies or between agglutinins and opsonins.

If a claim is made that there is a specific streptococcus for scarlet fever, a similar claim may be made for every other streptococcus, says Kolmer. The streptococcus found in scarlet fever belongs to the general class of streptococci, and is modified in some way during the course of the infection so as to give it a somewhat specific antibody and, occasionally, temporary cultural characteristics. This is also true of streptococci causing septicemia and simple sore throat. The reports of Russian physicians regarding the efficacy of injections of streptococcus vaccine, although apparently convincing, should be viewed with skepticism.

M. Nicoll, Jr., in discussing the paper read by Kolmer, stated that after a large experience in the use of antistreptococcus serum, he does not advise it except in cases resembling general septicemia. However, he has found that the local application of antistreptococcus serum to the mucous membrane of the pharynx and tonsils, frequently and freely applied, produced beneficial results.

## DIPHTHERIA

### HIGH DEATH-RATE OF DIPHTHERIA IN THE UNITED STATES

Hill<sup>20</sup> calls attention to the unnecessarily high death-rate from diphtheria in the United States. In practically every state in the union the percentage is high, averaging over twenty-five deaths per 100,000 as compared with only seven deaths per 100,000 in Paris. Hill believes that this is due to ineffective prophylactic measures, diagnoses made too late, and insufficient dosage of antitoxin in severe cases.

### STAPHYLOCOCCUS SPRAY IN DIPHTHERIA CARRIERS

Page<sup>21</sup> reports a case which he treated according to the ideas laid down by Schiötz in 1909. Schiötz noticed that patients with staphylococcus sore throats did not contract diphtheria if placed in the diphtheria wards,

20. Hill: Med. Record, April 1, 1911, p. 568.

21. Page: Arch. Int. Med., January, 1911, p. 16; New York Med. Jour., December 23, 1911.

and that staphylococcus sore throats often terminated positive diphtheria bacterial findings. Six diphtheria carriers were treated by sprays of a pure culture of *Staphylococcus aureus* with marked success.

Page's case was a diphtheria convalescent whose throat contained virulent bacilli three months after clinical symptoms had vanished. The staphylococcus culture was used as a spray every two hours, and on the third day the bacilli could no longer be found.

Catlin, Scott and Day<sup>22</sup> employed this procedure in eight nurses who were carrying diphtheria in spite of all treatment. All of the cases yielded to this method of treatment in a short time.

Up to the present the results have been remarkably successful and no harmful results have been caused by the staphylococcus.

#### ACTIVE IMMUNITY AGAINST DIPHTHERIA

Blumenau,<sup>23</sup> Dershovsky and Boldireff<sup>24</sup> and other Russian observers, by subcutaneous injections and local applications of diphtheria toxin to the nares, have produced active immunity to diphtheria in a number of cases. Small doses of the toxin were employed and the immunity was of longer standing than in cases which have received passive immunization with antitoxin.

#### ACETONURIA IN DIPHTHERIA

F. Reich<sup>25</sup> examined the urine in 3,200 cases of diphtheria and found acetone, by the sodium nitropruside test, present in 65 per cent. of the cases. Its frequency showed a direct relation to the severity of the attack, as it was present in 57.4 per cent. of the mild, 71.1 per cent. of the moderate and 80.3 per cent. of the severest cases. As it was found in 40.2 per cent. of non-diphtheritic throat inflammations its value as a diagnostic sign cannot be considered of great importance.

#### BLOOD-PRESSURE IN DIPHTHERIA

Rolleston<sup>26</sup> in a series of 179 cases of diphtheria found the blood-pressure subnormal in sixty-three patients, or 35.1 per cent., the extent and duration of the depression having, as a rule, a direct relation to the severity of the infection. High readings were obtained in the laryngeal and uremic cases. He concludes that sphygmomanometry in diphtheria, as in other acute disease, though of considerable theoretical interest, has little practical significance.

22. Catlin, Scott and Day: Jour. Am. Med. Assn., Oct. 28, 1911, p. 1452.

23. Blumenau: Vratsh, 1911, No. 5.

24. Dershovsky and Boldireff: New York Med. Record, May 6, 1911, p. 819.

25. Reich: München. med. Wehnschr., 1911, lviii, 2153.

26. Rolleston: Brit. Jour. Child. Dis., 1911, viii, 433.

L. L. Smith<sup>27</sup> reports a case of vulvovaginitis resembling gonorrhea in a 3-year-old girl. Smears from the mucopurulent discharge showed a pure culture of diphtheria bacilli. The throat was clear. Seven thousand units of antitoxin were given in the course of a few days and the inflammation subsided. The source of infection in this case was probably a bath towel used by a visitor who had been exposed to diphtheria and was suffering from a "cold" during her stay.

#### NASAL DIPHTHERIA

De Biehler and Dazskiewicz<sup>28</sup> report seven cases of apparently simple coryza, with few constitutional symptoms, which were really due to diphtheria, and were cured by antitoxin. They believe that the condition is more common than is supposed and urge the employment of cultures in cases in which operation is being considered and in persistent coryza.

#### GANGRENE FOLLOWING DIPHTHERIA

Ransome and Corner<sup>29</sup> and H. Kramer<sup>30</sup> report cases of gangrene of the leg in the second week of diphtheria.

#### ORGANOTHERAPY IN SERUM DISEASE

R. Wallace<sup>31</sup> suggests that the sudden death which may occur after the injection of serum into sensitized persons or those subject to bronchial asthma, is due to insufficiency of the suprarenal glands. He recommends the hypodermic injection of suprarenalin (adrenalin) both as a prophylactic and curative measure.

Hodgson<sup>32</sup> attempted to attenuate or prevent manifestation of serum sickness after injection of antitoxin by the administration of thyroid extract in small doses for four to six days. In about fifty cases this procedure appeared to have a good effect as compared with fifty cases in which the gland substance was not used.

#### VINCENT'S ANGINA ORGANISMS IN OTHER DISEASES

Blühdorn<sup>33</sup> examined smears from the throats of 222 patients, including cases of sore throat in various diseases, and healthy mouths, for the spirilla and fusiform bacilli present in Vincent's angina. He found both organisms, or one of them in

49 out of 76 cases of diphtheria.

11 out of 42 cases of scarlet fever.

27. Smith, L. L.: *New York Med. Jour.*, 1911, i, 24.

28. DeBiehler and Dazskiewicz, *Arch. de méd. d. enf.*, November, 1911.

29. Ransome and Corner: *Lancet*, London, 1911, i, 94.

30. Kramer: *Brit. Med. Jour.*, 1911, ii, p. 505.

31. Wallace: *Med. Rec.*, New York, Jan. 7, 1911, p. 15.

32. Hodgson: *Lancet*, London, 1911, clxxx, 373.

33. Blühdorn: *Deutsch. med. Wehnschr.*, June 22, 1911, xxxvii.

13 out of 26 cases of sore throat due to staphylococci and streptococci.

2 out of 4 cases of ulcerative stomatitis.

21 out of 31 cases of syphilis of mouth and throat.

22 out of 40 cases of healthy mouths.

These results make it evident that the clinical picture and smear may be inconclusive. Diphtheria must be excluded by a culture in every case.

#### DIPHTHERIA ANTITOXIN BY MOUTH

Cumberledge<sup>34</sup> has obtained good results with the oral administration of antitoxin. Results were obtained within a few hours, the patients showed no signs of serum sickness and were also spared the pain and discomfort of a hypodermic injection. An average of 2,000 units was given, and in some cases as a mixture in small dosage every two to four hours.

#### CHICKEN-POX

Magnan and de la Riboisière<sup>35</sup> report that they have found a fine Gram-negative bacillus in the vesicle of chicken-pox. The culture of the bacillus has been without result so far.

#### EPIDEMIC OF VARICELLA

Bondy<sup>36</sup> had the opportunity of observing an epidemic of chicken-pox in an orphanage at Warsaw. Of eighty-three infants, most of them under 6 months of age, twenty-seven were infected with the disease. A diffuse erythematous rash was observed one or two days before the varicella lesions appeared in eight cases, five of which resembled scarlet fever and three measles. No eruption was found on the mucous membrane of the mouth or throat. In some atrophic children, abscesses developed on the site of the lesion, which in two cases led to death from general sepsis. In three out of four cases complicated by measles the patients died of bronchopneumonia.

Luth<sup>37</sup> reports a case of herpes zoster in a woman whose baby was shortly after taken sick with chicken-pox. This close association of the two diseases has often been observed and the author does not believe that the connection is purely accidental.

#### WHOOPING COUGH

Wernstedt,<sup>38</sup> in a recent epidemic of pertussis, found a close and constant connection between the spasmophilic diathesis and the severe

34. Cumberledge: *Brit. Med. Jour.*, July 8, 1911.

35. Magnan and de la Riboisière: *Compt. rend. Soc. de biol.*, 1911, lxx, 309.

36. Bondy: *Przegląd Pedyatryczny*, 1911, iii, 177; *Abstr. Ztschr. f. Kinderh.*, i, 7, p. 608, 1911.

37. Luth: *Monatsh. f. prakt. Dermat.*, 1911, lii, 622.

38. Wernstedt: *Hygeia*, Stockholm, lxiii, No. 7, *Abstr. Jour. Am. Med. Ann.*, 1911, p. 1652.

spasmodic coughing in pertussis. The severe forms of the latter, he believes, are indications of a neuropathic constitution.

Mehnert<sup>39</sup> believes that ordinary small-pox vaccination has an attenuating effect on the spasmodic cough in pertussis. He vaccinated his patients as soon as a diagnosis of whooping-cough was made, and as soon as the pustule appeared the paroxysms became milder and disappeared within fifteen days at a maximum.

#### TYPHOID FEVER

##### BASS-WATKINS TYPHOID AGGLUTINATION TEST IN CHILDREN

Menville<sup>40</sup> employed the Bass-Watkins typhoid agglutination test on some eighty children and obtained positive results in all cases that proved to be typhoid. He follows the procedure as recommended by the originators — one-quarter of a drop of blood is smeared on the middle of a glass slide in the usual manner. The blood is then ready to be examined at any time. To make the test one drop of water is dropped over the blood and the blood dissolves within a quarter of a minute. With the same dropper one drop of typhoid suspension is placed on the center of the diluted blood. The slide is gently agitated until the reaction has shown itself positive; or for two minutes before it is called negative. A strong positive reaction appears often within a half minute. In the presence of positive blood, the agglutination in the blood serum causes the typhoid bacilli to stick together and to collect into a fine or coarse grayish, granular sediment, visible to the naked eye. Rapidly formed coarse granules indicate a strong reaction and fine granules a weak one. Fluid that is uniformly cloudy and shows no granules denotes a negative reaction. The test is recommended because of its apparent reliability and the simplicity with which it can be carried out.

##### TYPHOID IN INFANTS

Achard and Flandrin<sup>41</sup> report a case of typhoid in an infant, the third in their experience. The child was 11 months old, breast-fed and ran a course of thirteen days with symptoms of fever and depression and gastro-intestinal disturbances. No typhoid was discerned in the neighborhood. They believe that typhoid would be considered a less rare condition if serodiagnostics measures were applied to infants more regularly.

Kaspar<sup>42</sup> describes a case in an infant 10 weeks old, beginning with suppuration in the knee joint. The pus aspirated showed pure cultures of typhoid bacilli, as did the urine.

39. Mehnert: *Jahrb. f. Kinderh.*, June, 1911, lxxiii, No. 6.

40. Menville: *Arch. Pediat.*, March, 1912.

41. Achard and Flandrin: *de Progrès méd.*, 1911, p. 277.

42. Kaspar: *Monatsch. f. Kinderh.*, 9, 1911, p. 953.

## MEASLES

## EXPERIMENTAL WORK

During the past year Goldberger and Anderson<sup>43</sup> have reported some interesting observations on the transmission of measles to monkeys.

In 1898 Chavigny reported a case of measles in a monkey which had been exposed to a keeper suffering from measles. Josias in attempting to produce the disease in monkeys by exposure to children with measles failed in all his experiments. Grünbaum in 1904 attempted to produce the disease in two chimpanzees without success, and concluded that he had probably conferred immunity, rather than transmitted infection. It is believed that monkeys alone, of the lower animals, are susceptible to measles, but further investigation may prove this to be an error, as the experiments of Goldberger and Anderson were often negative in their monkeys.

In the experiments of Anderson and Goldberger blood was taken from undoubted cases of measles, defibrinated, and injected in amounts varying from 2.5 c.c. to 5 c.c. into the peritoneal cavity, under the dura, and into the heart. Nine animals were injected with blood from four undoubted cases of measles. Four of the monkeys showed positive reactions, with variable results.

The rash in a typical case appeared about ten days after the inoculation, first on the scalp, extending downward over the abdomen, back and limbs within the next two days. On the third day the rash began to fade and on the sixth day was scarcely perceptible. The temperature curve was similar to that in the child, reaching its height with the appearance of the eruption and falling as the rash disappeared. As in children, the temperature curve varied in the different monkeys. Some of the animals showed involvement of the respiratory mucous membrane, as evidenced by sneezing and coughing. No observations regarding Koplik's spots are recorded.

From the experiments of Goldberger and Anderson it appears that the blood is especially infective just before and during the first twenty-four hours of the eruption, after which it becomes progressively less infective.

The virus is filterable and can be passed through a Berkefeld filter.

Experiments with the mouth and nose secretions show that these secretions are infective at the time the rash appears. In three experiments with the scales the results were negative.

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43. Goldberger and Anderson: *Pub. Health Rep.*, June 9, 1911, p. 847; *ibid.*, June 16, 1911, p. 887; *Jour. Am. Med. Assn.*, July 8, 1911, p. 113; Aug. 5, 1911, p. 476; Sept. 16, 1911, p. 971; Nov. 11, 1911, p. 1612.

Hektoen<sup>44</sup> later obtained results similar to those of Goldberger and Anderson and made observations regarding the blood-findings in the measles of monkeys. He found practically the same changes as in human measles. There is a preliminary leukocytosis followed by a leukopenia, chiefly of the polymorphonuclear neutrophils, the lymphocytes being relatively increased.

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44. Hektoen: Jour. Am. Med. Assn., Dec. 2, 1911.

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- Lymphadenitis in the Iliac Fossa. (Adeniti e adeno-flemmoni cella fossa iliaca.) V. Brun.  
Riforma med., March 30, 1912.
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- Albumin Milk: Technic and Indications for Its Use. F. W. Schultz.  
Jour. Lancet, April, 1912.
- Casein-Enriched Milk for Infants. (Verwendbarkeit caseinangereicherte Kuhmilch. Theoretische Ueberlegungen.) P. Heim and K. M. John.  
Ztschr. f. Kinderh., 1912, iv, No. 1.
- Iron Content of Goat's Milk. (Der Eisengehalt der Ziegenmilch.) S. McLean.  
Ztschr. f. Kinderh., 1912, iv, No. 2.
- Infant Feedings. W. D. Chapman.  
Illinois Med. Jour., May, 1912.
- Infant Feeding. T. H. Elliott.  
West Virginia Med. Jour., May, 1912.
- Infant Feeding with Undiluted Cow's Milk. W. B. Hanbidge.  
New York State Jour. Med., April, 1912.
- Synthetic Milk Medium. H. A. Whittaker.  
Am. Jour. Public Health, March, 1912.
- Opsonins in Human Milk and Cow's Milk. (Kvinnomjölkens och komjölkens opsoniner.) I. Jundell.  
Hygiea, Stockholm, March, 1912.
- Tests of Efficiency of Pasteurization of Milk under Practical Conditions. E. H. Schorer and M. J. Rosenau.  
Jour. Med. Research, April, 1912.
- Lactose Has No Diuretic Action Unless Liver is Insufficient. (De la valeur réelle du lactose comme diurétique.) A. Cramer.  
Rev. de méd., April, 1912.
- Observations on Infant Fed with Barley Water and Cow's Milk. R. C. Verley.  
Brit. Med. Jour., April 13, 1912.
- Experimental Research on Action of Different Kinds of Sugar. (Vergleichende Untersuchungen am Hunde über die Wirkung verschiedener Zuckerarten.) G. Sainmont.  
Monatschr. f. Kinderh. 1912, x, No. 11.
- Fat in the Stools. (Untersuchungen über Fettstühle.) H. von Hoesslin and T. Kashiwado.  
Deutsch. Arch. f. klin. Med., April 6, 1912.
- Digestion Lipemia. (Zur Frage der Verdauungslipämie.) P. Schulz.  
Ztschr. f. Kinderh., 1912, iv, No. 1.
- Amount of Food and Protein Required by Young Children. (Zum Nahrungsbedarf und Eiweissbedarf des Kindes jenseits des Säuglingsalters.) J. Stargarder.  
Arch. f. Kinderh., Feb. 24, 1912.
- Complete Balance Studies of Nitrogen, Sulphur, Phosphorus, Calcium and Magnesium in Intestinal Infantilism. F. H. McCrudden and H. L. Fales.  
Jour. Exper. Med., May, 1912.
- Effect of Fat and of Carbohydrate Diets on Excretion of Creatin in Cases of Retarded Development. F. H. McCrudden.  
Jour. Exper. Med., May, 1912.
- Metabolism with Congenital Occlusion of Bile Passages. (Verhalten des Stoffwechsels bei angeb. Verschluss der Gallenwege.) A. Niemann.  
Ztschr. f. Kinderh., 1912, iv, No. 2.
- Rachitis and the Blood-Producing Organs. II. (Das Blut bei Rachitis.) E. Aschanheim.  
Deutsch. Arch. f. kin. Med., April 6, 1912.

Rachitis with Multiple Deformities. (Rachitisme avec déformations excessives.) J. Comby.

Arch. de méd. des enf., April, 1912.

White versus Yellow Cod Liver Oil in Rachitis. (Ist der weisse Lebertran bei der Behandlung der Rachitis dem gelben gleichwertig?) J. A. Schabad and R. F. Sorochowitsch.

Arch. f. Kinderh., Feb. 24, 1912.

Metabolic Findings in Child with Myxedema. A. Loewy and P. Sommerfeld. Deutsch. Arch. f. klin. Med., 1912, cvi, No. 2.

#### DISEASES OF THE NEWLY-BORN

Blood Transfusion for Hemorrhagic Disease of Newborn: Use of External Jugular Vein in Infants. B. Vincent.

Boston Med. and Surg. Jour., April 25, 1912.

Transient Fever in the Newly Born. (Ueber transitorisches Fieber bei Neugeborenen.) A. v. Reuss. (Fieberhafte Temperaturen bei neugeborenen Kindern in den ersten Lebenstagen.) F. Heller.

Ztschr. f. Kinderh., 1912, iv, No. 1.

Varices in Esophagus Responsible for Melena in Newly Born Infant. (Fall von Melæna neonatorum, hervorgerufen durch Blutung aus angeborenen Phlebektasien des Oesophagus.) F. Vorpahl.

Arch. f. Gynäk., April 6, 1912.

An Emergency Cannula. Transfusion in a Thirty-Six-Hour Old Baby Suffering from Melena Neonatorum. Bertram M. Bernheim.

Jour. Am. Med. Assn., April 6, 1912.

#### ACUTE INFECTIOUS DISEASES

Acute Poliomyelitis and Allied Conditions. E. F. Buzzard.

Lancet, London, April 6, 1912.

Acute Poliomyelitis: Clinical Aspects with Special Reference to Rarer Lesions. J. H. Hess.

Illinois Med. Jour., May, 1912.

Clinical Aspect and Treatment of Acute Anterior Poliomyelitis. C. M. Jacobs. Illinois Med. Jour., May, 1912.

Clinical Contribution to Our Knowledge of Poliomyelitis with Cortical Involvement. L. P. Clark.

Am. Jour. Med. Sc., April, 1912.

Epidemic Poliomyelitis: Clinical Study of Acute Stage. R. Stein.

Am. Jour. Med. Sc., April, 1912.

Etiology, Pathology and Treatment of Infantile Paralysis. L. E. Andrews.

Jour. Oklahoma Med. Assn., May, 1912.

Experimental Epidemic Poliomyelitis. (Experimentelle Poliomyelitis acuta.) M. Neustadter and W. C. Thro.

Deutsch. med. Wchnschr., April 11, 1912.

Infantile Paralysis (Acute Anterior Poliomyelitis). C. Thompson.

Louisville Month. Jour. Med. and Surg., April, 1912.

Pain as Symptom of Epidemic Poliomyelitis. (Die Schmerzsymptome der Heine-Medinschen Krankheit.) E. Tezner.

Monatschr. f. Kinderh., 1912, x, No. 11.

Pathology of Poliomyelitis. J. W. Jobling.

Illinois Med. Jour., May, 1912.

Poliomyelitis. L. D. Wilson.

West Virginia Med. Jour., May, 1912.

Prophylaxis of Epidemic Poliomyelitis and Treatment of the Conditions it Leaves. (Prophylaxe der Poliomyelitis acuta und die Behandlung ihrer Folgezustände.) E. Popper.

Centralbl. f. d. Grenzgeb. d. Med. u. Chir., March 23, 1912.

- Recent Contributions to Infantile Paralysis. M. W. Richardson.  
Am. Jour. Public Health, March, 1912.
- Symptomatology of Infantile Paralysis. J. V. Manning.  
Am. Jour. Obst., April, 1912.
- Surgical Aspects of Poliomyelitis. D. D. Lewis.  
Illinois Med. Jour., May, 1912.
- Contagious Period of Scarlet Fever. (Zur Infektionsdauer des Scharlachs.) A. Baginsky.  
Deutsch. Arch. f. klin. Med., 1912, cvi, No. 1.
- Diagnosis of Atypical Scarlet Fever. D. J. M. Miller.  
Arch. Pediat., April, 1912.
- Rumpell-Leede Phenomenon of Scarlet Fever. M. Michael.  
Arch. Pediat., April, 1912.
- Scarlet Fever. W. L. Welsh.  
Jour. Kansas Med. Soc., April, 1912.
- Serotherapy of Scarlet Fever. (Behandlung des Scharlachs mit Moser-Serum.) B. Schick.  
Therap. Monatsh., April, 1912.
- Serotherapy (Serum from Convalescents) in Scarlet Fever. (Behandlung schwerer Scharlachfälle mit Rekonvalescentenserum.) E. Reiss and P. Jungmann.  
Deutsch. Arch. f. klin. Med., 1912, cvi, No. 1.
- Some Clinical Features of Scarlatina. H. W. Berg.  
Med. Rec., New York, May 11, 1912.
- Vasomotor Ataxia Following Scarlet Fever. (Funktionsstörungen des Blut—und Lymphgefäßsystems der Haut als Folge des Scharlachexanthems. Beziehungen derselben zur Scharlach-Nephritis und Hautwassersucht.) O. Kirsch.  
Ztschr. f. Kinderh., 1912, iv, No. 2.
- Cerebrospinal Meningitis. W. L. Mosby.  
Kentucky Med. Jour., April, 1912.
- Cerebrospinal Meningitis Caused by Acid in Blood. D. G. Hall.  
Boston Med. and Surg. Jour., May 2, 1912.
- Etiologic and Epidemiologic Irregularities of Cerebrospinal Meningitis. H. D. King.  
New Orleans Med. and Surg. Jour., April, 1912.
- Influenzal Meningitis and Pneumonia. (Ytterlige bidrag till frågan om influensans etiologi och patologi.) I. Jundell.  
Hygiea, Stockholm, March, 1912.
- Meningitis, Special Reference to Diagnosis. A. O. Albin.  
West Virginia Med. Jour., May, 1912.
- Serotherapy of Cerebrospinal Meningitis. S. H. Landrum.  
Jour. Oklahoma Med. Assn., May, 1912.
- Treatment of Meningitis. A. C. Hirshfield.  
Jour. Oklahoma Med. Assn., May, 1912.
- Atypical Measles. (Epidémie de rougeole en 1905.) Fédon.  
Arch. de méd. des enf., April, 1912.
- Experimental Study of Measles in Monkeys. W. P. Lucas and E. L. Prizer.  
Jour. Med. Research, April, 1912.
- Measles. L. A. Clary.  
Jour. Kansas Med. Soc., April, 1912.
- Contact Infection in Contagious Diseases. B. Van D. Hedges.  
Arch. Pediat., April, 1912.
- Prevention of Commoner Contagious Diseases of Infancy and Childhood. R. S. Haynes.  
Arch. Pediat., April, 1912.
- Bronchopneumonia in Children. H. A. Hoyt.  
New York State Jour. Med., April, 1912.

- Epidemic Parotitis and Secondary Meningitis. (Zur Polymorphie der Parotitis epidemica mit bes Berücksichtigung secundärer Meningitiden.) H. Zade.  
Arch. f. Kinderh., Feb. 24, 1912.
- Erythema with Malignant Syndrome in Infectious Diseases. V. Hutinel.  
Ann. de méd. et chir. inf., April 1, 1912.
- Etiology and Symptoms of Chorea Minor. A. Westphal.  
Med. Klin., April 14, 1912.
- Examination of Cerebrospinal Fluid. A. D. Dunn and G. A. Stevens.  
Interstate Med. Jour., April, 1912.
- Fatal Generalized Vaccinia. (Cas de vaccine généralisée terminé par la moit.) L. d'Astros.  
Ann. de méd. et chir. inf., April 15, 1912.
- Is There any Valid Objection to Vaccination? C. W. Banks.  
Arch. Pediat., April, 1912.
- Scarlatinal Otitis Media. (Om otitis media perforative vid scarlatina.) G. Holmgren. To be continued.  
Hygiea, Stockholm, March, 1912.
- Threatening Anaphylaxis After Third Injection of Antitoxin in Eleven Years. (Todesgefahr infolge von Anaphylaxie.) W. Asam.  
Deutsch. med. Wehnschr., April 9, 1912.
- Treatment of Diphtheria. (Behandlung der Diphtherie.) E. Feer.  
Deutsch. med. Wehnschr., April 4, 1912.
- Epidemic of Sore Throat Due to Milk. A Preliminary Note. J. L. Miller and J. A. Capps.  
Jour. Am. Med. Assn., April 13, 1912.
- An Epidemic of Septic Sore Throat in Baltimore and Its Relation to a Milk Supply. A Preliminary Note. Louis P. Hamburger.  
Jour. Am. Med. Assn., April 13, 1912.

### TUBERCULOSIS AND SYPHILIS

- Anasarca without Albuminuria or Heart Disease in Child of Eight with Inherited Syphilitic Taint. Deléarde and Repellin.  
Arch. de méd. des inf., April, 1912.
- Creosote and Calcium Medication in Respiratory Affections in Children and in Pulmonary Tuberculosis. I. Van Gieson and H. L. Lynah.  
Med. Rec., New York, May 11, 1912.
- Hereditary Syphilis and Its Treatment by Salvarsan. J. L. Bunch.  
Brit. Jour. Child. Dis., April, 1912.
- Jaundice with Inherited Syphilis; Four Cases. (Ueber Ikterus bei der hereditären Syphilis.) O. Rosenberg.  
Deutsch. Arch. f. klin. Med., 1912, cvi, No. 2.
- Salvarsan in Inherited Syphilis. E. Andronescu.  
Deutsch. Arch. f. klin. Med., 1912, cvi, No. 2.
- Wassermann Reaction in Diagnosis of Inherited Syphilis. E. Andronescu and F. Saratzano.  
Presse méd., April 3, 1912.
- Curable Tuberculous Meningitis. (Des épisodes méningés tuberculeux curables.) H. Barbier and G. Gougelet.  
Arch. de méd. d. enf., April, 1912.
- Heredity and Feeding as Factors in Tuberculosis in Calves. (Sur la part de l'hérédité et de l'allaitement dans la tuberculose du veau. Indications relatives à la pathologie humaine.) M. Chausse and I. M. Benjamin.  
Bull. de l'Acad. de méd., Paris, April 2, 1912.
- Relations Between Human and Bovine Tuberculosis. (Beziehungen zwischen menschlicher und tierischer Tuberkulose.) H. Kossel.  
Deutsch. Arch. f. klin. Med., 1912, cvi, No. 1.

- Sunlight Treatment of Surgical Tuberculosis. (L'héliothérapie par la méthode de Rollier dans les tuberculoses chirurgicales.) P. F. Armand-Delille.  
Bull. Soc. de pédiat., March, 1912.
- Treatment of Tuberculous Peritonitis. (Traitement moderne de la péritonite tuberculeuse.) E. Périer.  
Ann. de méd. et chir. inf., April 15, 1912.
- Tuberculous Infection in Infancy and Childhood as Revealed by Cutaneous Tuberculin Test. C. McNeil.  
Edinburgh Med. Jour., April, 1912.

### DIGESTIVE SYSTEM

- Cirrhosis of the Liver in Child. (Cirrhose de Hanot chez un enfant. Infantile consécutif.) Pagliano and de Luna.  
Ann. de méd. et chir. inf., April 1, 1912.
- Congenital Anomalies of Appendix. R. McPherson.  
Bull. Lying-in Hosp., March, 1912.
- Congenital Malposition of Gall-Bladder. A. J. Walton.  
Lancet, London, April 6, 1912.
- Factors in Spread of Acute Intestinal Infections. H. W. Hill.  
Pub. Health Jour., April, 1912.
- Fatal Duodenal Ulcer in Young Infant. (Ulcère du duodénum chez un enfant d'un mois mort par hémorragie intestinale.) Weill and Gardère.  
Ann. de méd. et chir. inf., April 15, 1912.
- Hydrochloric Acid in Infant's Stomach. (Zalzsäure im Säuglingsmagen.) B. Salge.  
Ztschr. f. Kinderh., 1912, iv, No. 2.
- Imperforate Anus. A. A. Law.  
Jour.-Lancet, April 15, 1912.
- Intestinal Stasis in Children and Its Surgical Treatment. L. E. B. Ward.  
Practitioner, London, April, 1912.
- Pneumococcal Peritonitis in Children. S. Barling.  
Practitioner, London, April, 1912.
- Seroreaction in Alimentary Intoxication in Infants. (Reaktion des Blutserums bei alimentärer Seroreaktion des Säuglings.)  
Ztschr. f. Kinderkr., 1912, iv, No. 1.
- Stenosis of the Pylorus in Infants. (Estenosis pilorica en el lactante.) M. F. Cotignola.  
Semana méd., March 7, 1912.
- Surgical Treatment of Congenital Hypertrophic Pyloric Stenosis, with Report of Case. G. E. Gavin.  
Southern Med. Jour., May, 1912.
- Valve Ileus in Little Boy. (Ventilverschluss durch Abknickung im untersten Teil des Dickdarms in späteren Kindersalter.) F. Güppert.  
Berl. klin. Wehnschr., March 25, 1912.
- Congenital Dilatation of Colon, Megacolon or Hirschsprung's Disease. C. M. Rees.  
Jour. South Carolina Med. Assn., April, 1912.

### RESPIRATORY SYSTEM

- Case of Retained Tracheotomy Tube and Laryngeal Stenosis. P. S. Webster and S. W. Ferguson.  
Australian Med. Jour., March 9, 1912.
- Dilatation of Bronchial Tubes in Children. T. Fisher.  
Clin. Jour., April 3, 1912.
- Foreign Body Impacted in Bifurcation of Left Bronchus of a Boy. (Removal.) R. A. Stirling.  
Australian Med. Jour., Mar. 23, 1912.

Hernia of Lung From Absence of Left Sternocleidomastoid Muscle. (Hémiatrophie congénitale de la face et de la langue à gauche. Absence du muscle sterno-cleido-mastoidien et hernie cervicale du même côté.) G. Variot.

Bull. Soc. de pédiat., March, 1912.

Psychic and Organic Impediments to Removal of Trachea Tube. (Ueber psychisch bedingt Hindernisse für das Dekantlement und die Extubation.) I. Wickman.

Monatschr. f. Kinderh., 1912, x, No. 11.

Secondary Intubation for Organic Stenosis. I. Wickman.

Monatschr. f. Kinderh., 1912, x, No. 11.

### BLOOD AND CIRCULATORY SYSTEM

Blood in Infancy and Childhood. W. D. Ludlum.

Am. Jour. Obst., April, 1912.

Cardiac Disease in Children. R. O. Moon.

Clin. Jour., April 3, 1912.

Research on Blood Platelets. (Specifische Blutplättchen und die Theorie der directen reactiven Aufeinanderwirkung.) P. P. Eminent.

Arch. f. Kinderh., Feb. 24, 1912.

### NERVOUS SYSTEM

Arrest of Severe Epilepsy in Child Aged Four. J. S. Mackintosh.

Brit. Med. Jour., April 20, 1912.

Prevention of Epilepsy. M. L. Perry.

Jour. Missouri Med. Assn., April, 1912.

Surgery in Epilepsy. W. A. Bryan.

Southern Med. Jour., May, 1912.

What New Jersey is Doing for the Epileptic. D. F. Weeks.

Arch. Pediat., April, 1912.

Anorexia as Monosymptomatic Hysteria in Girl of 12. (Et tilfælde af infantil Hysteri.) G. Jorgensen.

Ugesk. f. Læger, April 4, 1912.

Clinical Importance of Conditional Reflexes in Children. (Bedingte Reflexe bei Kindern und ihre klinische Bedeutung.) E. Moro.

Therap. d. Gegenw., April, 1912.

Conditions of Irritation in the Sympathetic Nervous System in Infants. (Anteilnahme des sympathischen Nervensystems an den Erkrankungen des Säuglings. I.) F. Boschau.

Monatschr. f. Kinderh., 1912, x, No. 11.

Cure of Infantile Beriberi by Administration to Infant of Extract of Rice Polishings and The Bearing Thereof on Etiology of Beriberi. W. P. Chamberlain and E. B. Vedder.

Bull. Manila Med. Soc., February, 1912.

Erb's Palsy. H. W. Frauenthal.

Am. Jour. Obst., April, 1912.

Influence of Development of Brain on Nose and Face. J. M. Ingersoll.

Ohio State Med. Jour., April 15, 1912.

Nervous and Mental Disorders in Schools. A. W. Fairbanks.

Boston Med. and Surg. Jour., April 25, 1912.

Paramyoclonus from Mumps. (Paramyoclonus d'origine ourlienne.) M. Lafforgue.

Rev. de méd., April, 1912.

Treatment of Rumination in Infants. (Zur Therapie der Rumination im Säuglingsalter.) E. Mayerhofer.

Therap. Monatsh., April, 1912.

Case of Hysteria in Girl of Thirteen Years, Illustrating Mechanism of an Hallucination. R. Reed.

New York Med. Jour., May 11, 1912.

- Classification, Management, Education and Medical Treatment of the Feeble-Minded. M. Bannister.  
 Jour. Iowa. Med. Soc., March, 1912.
- Feeble-Minded: Classification and Importance. H. Sutton.  
 Australasian Med. Gaz., Jan. 13, 1912.
- Feeble-Mindedness and Measurement of Intelligence by Method of Binet and Simon. W. C. Sullivan.  
 Lancet, London, March 23, 1912.
- Juvenile Delinquency. E. B. McCready.  
 Dietet. and Hyg. Gaz., March, 1912.
- Scientific Aspect of the Backward Child. M. Freiman.  
 Dietet. and Hyg. Gaz., March, 1912.
- Subnormal Child in School, M. P. Doyle.  
 Virginia Med. Semi-Month., March 22, 1912.
- Dementia Præcox in Children. (La démence précoce dans l'enfance.) P. Haus-halter.  
 Arch. de Méd. d. enf., Paris, 1912, xv.
- Freud's Psychology as Applied to Children. W. E. Paul.  
 Boston Med. and Surg. Jour., April 4, 1912.
- Importance of Lumbar Puncture in Plumbic Ocular Neuritis of Children. J. L. Gibson.  
 Australasian Med. Gaz., Jan. 13, 1912.
- Juvenile Tabes. G. E. Price and C. E. G. Shannon.  
 AM. JOUR. DIS. CHILD., April, 1912.
- Mental Anorexia in Infants. (Anorexie mentale chez les nourrissons.) Buffet-Delmas.  
 Arch. de Méd. d. enf., Paris, 1912, xv, No. 3.
- Neurologic Aspect of the Period Including Puberty. (Das Entwicklungsalter von neurologischem Standpunkt.) W. v. Holst.  
 St. Petersburg. med. Wchnschr., Feb. 28, 1912.
- Operative Treatment of Epilepsy. (Zur Technik und Kasuistik der Epilepsieoperationen). Doberer.  
 Wien. klin. Wchnschr., March 7, 1912.

# GENITO-URINARY SYSTEM

- Exstrophy of the Bladder. (Étude anatomo-pathologique de l'exstrophie complète de la vessie.) Hovelacque. Commenced in No. 1.  
 Jour. d'Urol. méd. et Chir., Paris, 1912, xxx, No. 2.
- Kidney Calculi in Children. (Zur Frage des Salvarsanfiebers.) H. Hecht.  
 Med. Klin., March 10, 1912.
- Malignant Renal Tumor of Congenital Origin in Childhood: Report of Two Cases. J. L. Bendell.  
 Albany Med. Ann., March, 1912.
- The Relations between Phimosis and Kidney Disease. (Beziehungen zwischen Phimose und Nierenerkrankungen.) P. Heinrichsdorff.  
 Mitt. a. d. Grenzgeb. d. Med. u. Chir., March, 1912.
- Treatment of Undescended Testicle. (Procédé d'orchidopexie.) C. Walther and C. Monod.  
 Bull. de l'Acad. de méd., Paris, March, 1912.
- Congenital Malformations of Ureters. D. N. Eisendrath.  
 Ann. Surg., April, 1912.
- Hemorrhagic Nephritis in Infant with Inherited Syphilis. R. Hahn.  
 Deutsch. Arch. f. klin. Med., 1912, cvi, No. 2.
- Intensity of Acidity of Urine in Children. G. King.  
 Boston Med. and Surg. Jour., May 9, 1912.

## OSSEOUS SYSTEM

- Abbott's Method of Correcting Fixed Lateral Curvature. D. D. Ashley.  
New York Med. Jour., April 27, 1912.
- Correction of Lateral Curvature of Spine. E. G. Abbott.  
New York Med. Jour., April 27, 1912.
- Rotary Lateral Curvature on Report of Results Obtained. C. Ogilvy.  
New York Med. Jour., April 27, 1912.
- Acute Osteomyelitis of the Upper Jaw in Three-Weeks' Infant. H. Fliess.  
Arch. f. Kinderh., Feb. 24, 1912.
- Economic Value of Deciduous Teeth. M. E. Jordan.  
California State Jour. Med., April, 1912.
- Sarcoma of Upper Jaw in Infant under Two. H. L. Rocher.  
Rev. mens. de gynec. d'obst. et de pédiat., Paris, March, 1912.
- Common Deformities in Hip Disease: Their Treatment and Correction. A. O'Reilly.  
Jour. Missouri Med. Assn., April, 1912.
- Congenital Dislocation of Hip. F. J. Fassett.  
Northwest Med., April, 1912.
- Congenital Dislocation of Hip-Joint. (La luxation congénitale de la hanche.)  
P. Le Damany.  
Arch. gén. de chir., March 25, 1912.
- Local Surgical Procedures in Non-Tuberculous Joint Diseases. E. H. Ochsner.  
Illinois Med. Jour., May, 1912.
- Operation for Pott's Disease of Spine. R. A. Hibbs.  
Ann. Surg., May, 1912.
- Osteoplasty and Bone Transplantation in Pott's Disease of Spine. F. H. Albee.  
Vermont Med. Month., April 15, 1912.
- Orthopedic Defects and Rickets. J. E. Goldthwait.  
Boston Med. and Surg. Jour., April 25, 1912.
- Idiopathic and Symptomatic Genu-Valgum. (Genu-valgum essentiel et genu-valgum symptomatique.) E. Kirmisson.  
Presse méd., April 10, 1912.

## SKIN AND APPENDAGES

- Infantile Eczema. C. A. Simpson.  
Jour. Am. Med. Assn., April 6, 1912.
- Skin Lesions in Child from Bromid Poisoning. (Bromides papulo-tuberculeuses géantes.) J. Hallé and Dorlencourt.  
Bull. Soc. Pédiat., Paris, 1912, xiv, No. 2.
- Skin Rashes in Children. J. L. Bunch.  
Brit. Med. Jour., March 30, 1912.
- A Case of Extensive Pigmented and Hairy Nevus of the "Bathing-Trunk" Type, Presenting Genital Tumors. Howard Fox.  
Jour. Am. Med. Assn., April 20, 1912.

## EYE, EAR, NOSE AND THROAT

- Case of Antral Disease in Four-Months-Old Child, with Marked Orbital Symptoms. F. Krauss.  
Arch. Ophth., March, 1912.
- Direct Laryngoscopy, Bronchoscopy and Esophagoscopy. P. Watson-Williams.  
Bristol Med.-Chir. Jour., March, 1912.
- Laryngospasm in Infant from Intranasal Instillation of Resorcin in Oil. G. Railliet.  
Bull. Soc. de pédiat. de Paris, 1912, xiv, No. 2.
- Method of Enucleation of Tonsils. C. W. M. Hope.  
Brit. Med. Jour., March 9, 1912.
- Plasma Cells in Tonsils. D. J. Davis.  
Jour. Infect. Dis., March, 1912.



- Tonsillectomy: With Presentation of Specimens Removed by Author's Method. G. Sluder.  
 Jour. Missouri Med. Assn., March, 1912.
- Medical Treatment of Strabismus. J. Comby.  
 Bull. de l'Acad. de méd., Paris, March 26, 1912.
- Strabismus in Children. J. L. Dickey.  
 West Virginia Med. Jour., May, 1912.
- Lymphatic Apparatus of Nose and Naso-Pharynx in Its Relation to Rest and Body. Three papers. J. Broeckaert, C. Poli, A. L. Turner.  
 Laryngoscope, March, 1912.
- Lymphatics of Nose and Naso-Pharynx with Consideration of General Lymphatic System. H. J. Hartz.  
 Laryngoscope, March, 1912.
- Position of Patient for Throat and Nasal Operations under Local and General Anesthesia. M. D. Stevenson.  
 Ohio State Med. Jour., April 15, 1912.
- Cleft Palate. T. W. Brophy.  
 Lancet-Clinic, April 20, 1912.
- Shield for Throat Examinations. (Ecran transparent fronto-facial pour l'examen de la gorge des enfants.) J. Renault.  
 Bull. Soc. de pédiat., March, 1912.
- Congenital Laryngeal Stridor: Report of Case. J. M. Ray.  
 Louisville Month. Jour. Med. and Surg., May 1912.
- Enlarged Tonsils and Why They Should Be Removed. H. T. Bailey.  
 New Mexico Med. Jour., April, 1912.
- Importance of Maintaining Normal Mouth Conditions in Children. J. C. Archer.  
 West Virginia Med. Jour., May, 1912.
- Improved Mouth-Gag for Tonsillectomy. H. B. Hitz.  
 Wisconsin Med. Jour., April, 1912.
- Tonsillectomy as Performed at Charity Hospital, New Orleans. H. Dupuy.  
 Southern Med. Jour., May, 1912.
- Malignant Pneumococcus Tonsillitis. Leonard K. Hirshberg.  
 Jour. Am. Med. Assn., April 20, 1912.
- Tonsil Guillotine with a Dull Blade. William E. Sauer.  
 Jour. Am. Med. Assn., May 4, 1912.
- Surgical Removal of Tonsils. Finger Enucleation. F. A. Foster.  
 Am. Jour. Surg., April, 1912.
- Importance of Early Diagnosis in Middle-Ear Disease in Children. G. A. Aschman.  
 West Virginia Med. Jour., May, 1912.

#### THERAPEUTICS

- Normal Human-Blood Serum in Obstetric and Pediatric Practice. J. E. Welch.  
 Am. Jour. Obst., April, 1912.
- Organotherapy for Backward Children. (Arriération infantile et opothérapie endocrinienne.) Dupuy.  
 Rev. de méd., April, 1912.
- Preliminary Serotherapy by the Mouth and in Local Application. (Sérothérapie antistreptococcique par voie buccale et en applications locales.) A. Darier.  
 Presse méd., April 10, 1912.

#### SURGERY

- Etiology of Talipes Cavus. (Zur Aetiologie des Klauenhohlfusses.) F. Geiges.  
 Beitr. z. klin. Chir., March, 1912.
- Two Unusual Cases of Hare-Lip. (2 cas de bec-de-lièvre pseudo-médian dont l'un compliqué d'anencéphalie.) A. Matthey.  
 Rev. méd. de la Suisse romande, February, 1912.
- Excellent Ultimate Results from Subcutaneous Tenotomy for Congenital Torticollis. A. Jalaguier and L. Lamy.  
 Bull. Soc. de pédiat., March, 1912.

- Hernia in Children. H. S. Pendlebury.  
Clin. Jour., April 3, 1912.
- Paralysis Complicating Fracture of Humerus in Two Children. (2 cas de paralysie radiale compliquant une fracture de l'extrémité inférieure de l'humérus.) Gallois and Tartanson.  
Lyon méd., April 7, 1912.
- Surgical Cases in Children. E. M. Corner.  
Clin. Jour., April 3, 1912.
- Thymectomy. (De la valeur et des indications opératoires de la thymectomie dans l'hypertrophie de thymus.) E. Olivier.  
Jour. de Chir., March, 1912.
- Treatment of Fractures at Elbow in Childhood. W. F. Campbell.  
Am. Jour. Obst., April, 1912.
- Hernia in Children. R. J. Reed.  
West Virginia Med. Jour., May, 1912.
- Tendon Transplantation and Silk Inserts. James Warren Sever.  
Jour. Am. Med. Assn., May 11, 1912.
- Arthrodesis of Some of the Smaller Joints in the Treatment of Paralytic and Acquired Deformities. Robert E. Soule.  
Jour. Am. Med. Assn., May 11, 1912.

## MISCELLANEOUS

- Effect of Heated Term on Infants and Older Children. (Einwirkung der Sommerhitze auf Säuglinge und ältere Kinder.) E. Schlesinger.  
Deutsch. med. Wchnschr., March, 1912.
- Feeding and Care of Infants of Poor. P. V. K. Johnson.  
South. California Pract., March, 1912.
- Inherited Morbidity. (Ueber Vererbung von Krankheiten.) B. Hirschfeld and F. Pick.  
Deutsch. med. Wchnschr., 1912, xxxviii, No. 11.
- Mortality During Great Heat of 1911. (Die Gesamtsterblichkeit und die "Säuglingssterblichkeit während des Hitzvierteljahres 1911 im preussischen Staat und speziell im Stadtkreis Berlin.) R. Behla.  
Berl. klin. Wchnschr., 1912, xlix, No. 11.
- Ten Years as Dental Surgeon to Children's Hospital. S. F. Rose.  
Brit. Jour. Dis. Child., March, 1912.
- The Children of Liquor Drinkers. (Die Trinkerkindern unter den schwachbegabten Schulkindern.) E. Schlesinger.  
München. med. Wchnschr., March, 1912.
- Conference on Diseases Among School Children and Remedy. E. O. Otis.  
Boston Med. and Surg. Jour., April 25, 1912.
- Duty of Community to Its Backward and Defective Children. I. T. Smart.  
Arch. Pediat., April, 1912.
- Infant Mortality During Heated Term. (Die Sommersterblichkeit der Säuglinge.) H. Reitschel.  
Med. Klin., April 14, 1912.
- Infants with Abnormally Large Abdomens. (Variations, sous l'influence de la ration alimentaire, du périmètre—susombilical—chez les nourrissons atteints d'ectasie abdominale.) G. Variot and Morance.  
Bull. Soc. de pédiat., March, 1912.
- Measures for Child Welfare in Russia. (Der gegenwärtige Stand der Frage über die Kindersterblichkeit in Russland und deren Bekämpfung.) W. Hubert.  
Arch. f. Kinderh., Feb. 24, 1912.
- New Public Children's Hospital. (Der Ausbau des städtischen Kaiser und Kaiserin-Friedrich-Kinderkrankenhauses in Berlin.) A. Baginsky and the Architects.  
Arch. f. Kinderh., Feb. 24, 1912.
- Value of Child Study. D. P. Macmillan.  
Chicago Med. Recorder, April 15, 1912.

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